# (11) **EP 1 770 171 A1**

(12)

## **EUROPEAN PATENT APPLICATION**

(43) Date of publication: 04.04.2007 Bulletin 2007/14

(51) Int Cl.: C12Q 1/68 (2006.01)

(21) Application number: 05109025.6

(22) Date of filing: 29.09.2005

(84) Designated Contracting States:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR

Designated Extension States:

AL BA HR MK YU

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- (54) DNA microarray for rapid identification of Candida albicans in blood cultures.
- (57) The present invention provides a DNA microarray for identification and characterisation of microorganisms in a sample or clinical specimen. Furthermore, it provides for a method for rapid identification and strain

profiling of different microbial species in clinical specimens, especially in blood cultures, utilizing said DNA microarray.

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### Description

**[0001]** The present invention provides a DNA microarray for identification and characterisation of microorganisms in a sample or clinical specimen. Furthermore, it provides for a method for rapid identification and strain profiling of different microbial species in clinical specimens, especially in blood cultures, utilizing said DNA microarray.

### Background

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nosocomial bloodstream infection.

**[0002]** Isolation, identification and characterisation of bacteria from clinical specimens is a main task of microbiological routine diagnostics. In fact, microorganisms are ubiquitous in certain areas of the human body. For this reason isolation and identification of pathogenic bacteria from clinical material and discrimination of specific pathogens from contaminations with indigenous or environmentally encountered microorganisms is a requirement for the correct diagnosis of infectious diseases. Additionally, accurate identification of antibiotic resistance and particular virulence factors provide important information enabling the clinician to choose effective antimicrobial therapy.

[0003] In the course of infection, many specimen types can be used for direct identification of the pathogens. These include, but are not limited to, liquor in the course of bacterial meningitis, sputum from patients with bacterial pneumonia, urine in the course of upper and lower urinary tract infections, punktate from sites of deep purulent infections (such as abscess, phlegmone, lung emphysema and septic arthritis), stool from patients with gastrointestinal tract infections, pus or wound fluid from purulent infections of the skin and wounds. Sometimes, bacteria are represented in the specimen only in minor numbers, thus, indirect identification of pathogens after culture of specimens in liquid media is employed. Important examples are enrichment cultures of food samples during outbreaks of food borne infections and blood cultures for diagnosis of bloodstream infections.

[0004] The invasion of the bloodstream by microorganisms, especially bacteremia and fungemia, represents one of the most serious consequences of infections and is a high ranked cause of death (Mylotte, J.M. and Tayara, A., Eur. Clin. Microbiol. Infect. Dis. 19:157-163 (2000); Reimer, L.G. et al., Clin. Microbiol. Rev. 10:444-465 (1997)). Bacteremia is the means by which local infections spread hematogenously to distant organs. This hematogenous dissemination of bacteria is part of the pathophysiology of, e.g., meningitis and endocarditis, Pott's disease and many other forms of osteomyelitis. In the hospital, indwelling catheters are a frequent cause of bacteremia and subsequent nosocomial infections, since they provide a means by which bacteria normally found on the skin can enter the bloodstream. Other causes of bacteremia include dental procedures, urinary tract infections, intravenous drug use, and colorectal cancer. [0005] Systemic fungal infection is becoming more and more common in modern hospitals. The most common fungal infections are candidiasis and aspergillosis, but other systemic fungal infections such as Histoplasmosis, Blastomycosis, Coccidioidomycosis and Cryptococcosis are also of increasing relevance. Systemic fungal infections in hospitals are commonly seen in immune compromised patients and - like bacteremia - in patients with indewelling catheters. Due to underlying serious illnesses and possible resistance of the pathogens to antifungal agents, patients with systemic fungal infections often have poor clinical outcomes. Infections due to Candida species are the fourth most important cause of

**[0006]** Bacteremia is operationally defined as the presence of viable bacteria as evidenced by positive blood cultures. Fungemia is similarly defined as the presence of viable fungi as evidenced by positive blood cultures. When bacteremia or fungemia occurs in the presence of systemic symptoms (such as fever or chills) the condition is designated as sepsis; and in the setting of more severe disturbances of temperature, respiration, heart rate or white blood cell count, is characterised as systemic inflammatory response syndrome (SLRS).

[0007] Many septic episodes are nosocomial and often due to microorganisms with increased and multiple antimicrobial resistance. *Staphylococcus aureus, Escherichia coli,* Coagulase-negative staphylococci (CoNS), *Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus* spp., *Streptococcus* spp., *Candida albicans* and *Enterobacter cloacae* are the most frequent etiological agents of bacteremia and fungemia in Europe (Decousser, J. W. et al., J. Antimicrob. Chemother. 51:1214-22 (2003); Lyytikainen, O. et al., Clin. Infect. Dis. 35:314-9 (2002); Reacher, M.H. et al., BMJ 320: 213-6 (2000); Rosenthal Kreuberger, E.J., Int. J. Antimicrob. Agents 24:196-8 (2004)) and the USA (Bourbeau, P.P. and Pohlman, J.K., J. Clin. Microbiol. 39:2079-82 (2001); Reimer, L.G. et al., Clin. Microbiol. Rev. 10:444-65 (1997); Reisner, L.G. et al., J. Clin. Microbiol. 37:1709-13 (1999)).

[0008] Nosocomial bacteremia and especially sepsis require an immediate antibiotic therapy, even when the causative bacteria are still unknown. Thus, said therapy has to be performed as empirical initial therapy (Rello, J. et al., Intensive Care Med. 20:94-98 (1994)), which covers the complete spectrum of relevant pathogens. However, the increase of bacterial resistance lowers the chance of success for such empirical antibiotic treatments considerably (Mylotte, J.M. and Tayara, A., Eur. Clin. Mcrobiol. Infect. Dis. 19:157-163 (2000); Weinstein, M.P. et al., Clin. Infect. Dis. 24:584-602 (1997)). This primary therapy can only be replaced by a specific treatment after a thorough microbial diagnosis which usually takes 76-120 h (Bourbeau, P.P. and Pohlman, J.K., J. Clin. Microbiol. 39:2079-2082 (2001)). A fast track diagnosis which shortens this lag time would increase the chance of therapy success.

[0009] Rapid and reliable detection of bloodstream infections, including characterisation of the pathogen to the species level and determination of its antibiotic susceptibility pattern, is crucial for several reasons: (i) Appropriate antimicrobial agents can be selected, and thus, unnecessary treatment with ineffective antibiotics can be avoided; (ii) the prognosis of the patients can be improved; (iii) the acquisition of resistances in pathogens may be decelerated and (iv) expenditures on antimicrobials and overall hospital costs can be reduced (Barenfanger, J. et al., J. Clin. Microbiol. 37:1415-8 (1999); Doern, G.V. et al., J. Clin. Microbiol. 32:1757-62 (1994); Trenholme, G.M. et al., J. Clin. Microbiol. 27:1342-5 (1989); Wheeler, A.P. and Bernard, G.R., N. Engl. J. Med. 340:207-14 (1999)). Therefore, there is a strong need for rapid tests for specific and sensitive identification of bacteria and pathogenic fungi directly from blood cultures.

[0010] The diagnosis of bacteremia commonly relies on blood cultures where the growth of microorganisms is continuously monitored by automated devices (James, P.A. and Al-Shafi, K.M., J. Clin. Pathol. 53:231-233 (2000); Reisner, B.S. and Woods, G.L., J. Clin. Microbiol. 37:2024-2026 (1999); Wilson, M.L. et al., J. Clin. Microbiol 37:1709-1713 (1999). Although such continuous-reading and computed systems decrease the time for detection of positive blood cultures, definitive pathogen identification from positive blood cultures still requires traditional Gram-staining, sub-culturing and susceptibility testing, delaying the identification of pathogens for one to three days (Levi, K and Towner, K.J., J. Clin. Microbiol. 41:3890-3892 (2003); Oliveira, K. et al., J. Clin. Microbiol. 41:889-891 (2003); Oliveira, K. et al., J. Clin. Microbiol. 40:247-251 (2002); Tan, T.Y. et al., J. Clin. Microbiol. 39:4529-4531 (2001)). The subculture procedure with subsequent species identification and determination of antibiotic resistance is time-consuming and elaborate. The biochemical and immunological assays like testing with coagulase, nuclease or latex agglutination are not always reliable. Antigenic and biochemical variations of bacteria grown in blood culture, inhibitory action of blood culture medium components as well as the presence of more than one microbial species may mislead data interpretation.

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[0011] Staphylococci are the most important and frequent group of pathogens growing in blood culture, responsible for 30% to more than 50% of all bacteremia events (James, P.A. and Al-Shafi, K.M., J. Clin. Pathol. 53:231-233 (2000); Reisner, B.S. and Woods, G.L., J. Clin. Microbiol. 37:2024-2026 (1999); Velasco, E. et al., Sao Paulo Med. J. 118: 131-138 (2000)) with a mortality rate ranging from 13 to 50% (McClelland, R.S. et al., Arch. Intern. Med. 159:1244-1247 (1999); Rello, J. et al., Intensive Care Med. 20:94-98 (1994); Weinstein, M.P. et al., Clin. Infect. Dis. 24:584-602 (1997)). The emergence of S. *aureus* strains with multiple resistance to antibiotics makes empirical therapy prone to fail (Tan, T.Y. et al., J. Clin. Microbiol. 39:4529-4531 (2001)). S. *aureus* is generally regarded as a virulent pathogen, whereas CoNS are either considered as a cause of catheter-associated nosocomial bacteremia or, more frequently, as blood culture contamination. Thus, a subgenus identification of gram-positive cocci in clusters (CPCC) is of great clinical significance (Oliveira, K. et al., J. Clin. Microbiol. 41:889-891 (2003)).

**[0012]** Methods used up to date for direct identification of *S. aureus* growing in blood culture bottles include biochemical tests, like detection of thermostable nuclease or tube coagulase test, or commercial antibody-based kits connected with the disadvantages listed above.

Esides *S. aureus* and coagulase-negative staphylococci, *E. coli, Klebsiella* spp., *Enterobacter* spp., *Proteus* spp. and *P. aeruginosa* belong to the most frequent reported pathogens causing bacteremia (Reimer, L.G. et al., Clin. Microbiol. Rev., 10:444-65 (1997); Reacher, M.H. et al., BMJ, 320:213-6 (2000); Lyytikainen, O. et al., Clin. Infect. Dis., 35:e14-9 (2002)). In order to reduce the time needed for identification and susceptibility testing, the possibility of combining an automated blood culture system with an automated identification and susceptibility testing system by direct inoculation from positive blood cultures has been studied for gram-positive cocci as well as for gram-negative rods by several groups of investigators, but with varying success (Reimer, L.G. et al., Clin. Microbiol. Rev., 10:444-65 (1997); Hansen, D.S. et al., Clin. Microbiol. Infect., 8:38-44 (2002); Ling, T.K. et al., J. Clin. Microbiol., 41:4705-7 (2003); Funke, G. and Funke-Kissling, P., J. Clin. Microbiol., 42:1466-70 (2004)). Although the authors saw some potential of the combined system to allow the agar isolation step to be skipped, the system is hampered by the fact that (i) the blood culture sample has to undergo a time-consuming separation procedure for the enrichment of bacterial cells, (ii) the identification rate varies depending on the employed identification system and (iii) the performance is not equally good for gram-negative and gram-positive pathogens (Reimer, L.G. et al., Clin. Microbiol. Rev., 10:444-65 (1997); Ling, T.K. et al., J. Clin. Microbiol., 41:4705-7 (2003); Funke, G. and Funke-Kissling, P., J. Clin. Microbiol., 42:1466-70 (2004)).

[0014] Considerable progress was made using nucleic acid-based methods for the identification and genotyping of bacteria or fungi in blood specimens. Assays employing ribosomal RNA-based oligonucleotide probes like fluorescence *in situ* hybridisation (FISH) (Chapin, K. and Musgnug, M., J. Clin. Microbiol. 41:4324-7 (2003); Jansen, G.J. et al., J. Clin. Microbiol. 38:830-8 (2000); Oliveira, K. et al., J. Clin. Microbiol. 41:489-91 (2003)) or microarrays (Anthony, R.M. et al., J. Clin. Microbiol. 38:781-8 (2000); Marlowe, E.M. et al., J. Clin. Microbiol. 41:5127-33 (2003); Sogaard, M. et al., J. Clin. Microbiol., 43:1947-9 (2005)) provide for rapid species identification in blood cultures. However, methods solely based on ribosomal RNA probes allow species identification only, and do not provide information on antibiotic susceptibility and other strain specific characteristics (e.g. virulence genes). For the molecular detection of antibiotic resistances in staphylococci, several multiplex PCR-based assays were described (Martineau, F. et al., Antimicrob. Agents Chemother. 44:231-8 (2000); Shrestha, N.K. et al., Approved standard M2-4A, Villanova, PA (1990); Strommenger, B.C. et al. J. Clin. Microbiol. 41:4089-94; Tan, T.Y. et al., J. Clin. Microbiol.

39:4529-31 (2001)). Several groups have successfully identified *S. aureus* and more specifically methicillin-resistant *S. aureus* strains (MRSA) from blood cultures by using DNA probes (Levi, K. and Towner, K.J., J. Clin. Microbiol. 41: 3890-3892 (2003); Poulsen, A.B. et al., J. Antimicrob. Chemother. 51:419-421 (2003)), peptide nucleic acid probes (Oliveira, K. et al., J. Clin. Microbiol. 41:889-891 (2003)), multiplex PCR (Mason, W. J. et al., J. Clin. Microbiol. 39: 3332-3338 (2001)), gel-based PCR(Krishnan, P.U. et al., J. Clin Pathol. 55:745-748 (2002)), and real-time PCR (Shrestha N.K. et al., J. Clin. Microbiol. 40:2659-2661 (2002); Tan, T.Y. et al., J. Clin. Microbiol. 39:4529-4531 (2001)).

**[0015]** However, the use of such molecular assays suffers from two main restrictions: First, they rely on a pre-identification of the pathogen since their discriminatory capacity is technically limited, for instance by the number of fluorochromes available for labelling the probes or, in the case of multiplex PCR, by the capacity of resolution in gel electrophoresis. These molecular assays are thus usually not scalable and unfit for high throughput analysis.

[0016] The last years have witnessed the emergence of many DNA microchip projects arraying genes of microorganisms (Ye, R.W. et al., J. Microbiol. Methods 47:257-272 (2001)). They can detect tens of thousands of DNA sequences in a single hybridisation step (DeRisi, J.L. et al., Science 278:680-686 (1997); Duggan, D.J. et al., Nat. Genet. 21:10-14 (1999); Lashkari, D.A. et al., Proc. Natl. Acad. Sci. USA 94:13057-13062 (1997)). Originally developed for gene expression profiling, DNA sequence analysis and genotyping, microarrays were recently also used to identify viral (Wang, R.F. et al., FEMS Microbiol. Lett. 213:175-182 (2002)) and bacterial (Bekal, S. et al., J. Clin. Microbiol. 41:2113-2125 (2003)) pathogens in environmental and clinical samples.

[0017] Most of the published reports employed oligonucleotide microarrays containing a reduced number of spotted probes and representing a single bacterial species only (Volokhov, D. et al., J. Appl. Microbiol. 95:787-798 (2003); Volokhov, D. et al., J. Clin. Microbiol. 41:4071-4080 (2003); Volokhov, D. et al., J. Clin. Microbiol. 40:4720-4728 (2002)). Such arrays were used to identify pathogenic strains belonging to a pre-identified species (Chizhikov, V. et al., Appl. Environ. Microbiol. 67:3258-3263 (2001)), to distinguish between species of the same genus (Volokhov, D. et al., J. Clin. Microbiol. 41:4071-4080 (2003); Volokhov, D. et al., J. Clin. Microbiol. 40:4720-4728 (2002)) or to detect genes encoding resistance to a certain antibiotic (Volokhov, D. et al., J. Appl. Microbiol. 95:787-798 (2003)).

[0018] Although such specific short-oligonucleotide microarrays could be rapidly designed and built up they carry some intrinsic disadvantages: like all methods based on single and often short DNA sequences they show reduced reliability and sensitivity (Stears, R.L. et al., Nat. Med. 9:140-145 (2003)). To palliate the high probability of non-specific hybridisation due to their short size (20-40bp) it is necessary to design many partially overlapping oligonucleotides in order to confirm the presence of a gene. This consequent increase in complexity makes it extremely difficult to set up the optimal hybridisation conditions necessary for producing trustful results. Moreover, surface-bound short oligonucleotides have poor hybridisation properties and are highly sensitive to single nucleotide polymorphisms (Hughes, T.R. et al., Nat. Biotechnol. 19:342-347 (2001)). For these reasons, oligonucleotide micro-arrays are unsuitable for routine diagnostics.

**[0019]** Up to now, diagnosis of bacteremia by microarrays is limited to species identification by oligonucleotides for 23S RNA sequences, which is still strictly experimental (Anthony, R.M. et al., J. Clin. Microbiol. 38:781-788 (2000)) and carries along the methodological weakness associated to the use of oligonucleotides as hybridisation probes.

[0020] A DNA microarray employing capture probes of more than 40 nt length amplified by PCR was described by Fitzgerald et al. (Fitzgerald, J.R. at al., Proc. Natl. Acad. Sci. USA 98(15):8821-8826 (2001)). To investigate molecular population genetics of *Staphylococcus aureus* on a genome scale, a microarray comprising 2817 complete ORFs of *S. aureus* strain COL was constructed, representing >90% of the *S. aureus* genome. The microarray was able to discriminate 36 *S. aureus* strains. However, since it was not designed for the identification of different bacterial species, it was not tested for possible cross reactions with other bacteria besides *S. aureus*. Due to the conservative nature of many house-keeping proteins and genes, respectively, cross reactions of the microarray with CoNS strains and other bacterial species will occur. Unspecific cross reactions combined with the high number of probes (2817) result in a high complexity of the microarray data, not applicable to routine diagnostics. Furthermore, PCR amplification of long ORFs is a difficult procedure, in particular for bacteria with DNA of high GC-content.

**[0021]** The aim of present invention is to provide a gene-segment based microarray for identification and characterisation of different microorganisms, especially different bacteria and pathogenic fungi, present in a sample or clinical specimen.

Summary of the Invention

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**[0022]** The present invention provides a DNA microarray for the identification and characterisation of microorganisms in biological samples, especially of microorganisms connected with bacteremia, fungemia and sepsis. Species specific gene probes in this microarray allow the identification of different microbial species, whilst antibiotic resistance and virulence gene probes allow for the genotypic discrimination within a species. The microarray can be designed to allow species identification, virulence determination and resistance determination independently from each other or simultaneously, and furthermore said determinations can be performed for one or more different microbial species and strains

with one microarray. Furthermore, different microbial species and strains are discriminated, even in a polymicrobial sample (specimen with more than one pathogen).

**[0023]** The DNA microarray according to present invention thus demonstrates the feasibility of simultaneously identifying and characterising different microbial species in a sample or clinical specimen, especially in blood samples, without prior PCR amplification of target DNA or pre-identification of the pathogen. This can reduce sample processing time to a single day and less.

**[0024]** The invention furthermore provides a method for rapid identification and characterisation of microorganisms, especially of bacteria, yeasts and filamentous fungi, using the microarray of the invention. The method is quick, can be automated, leads to reproducible results and allows an early choice of specific antibiotics for treatment of bacteremia, fungemia or sepsis.

[0025] In particular, the present invention provides

- (1) a DNA microarray for direct identification and characterisation of microorganisms in a sample or clinical specimen, wherein the microarray comprises gene probes being derived from DNA sequences or partial DNA sequences of the microorganisms to be identified or DNA sequences complementary or homologous thereto and having a length of at least 100 nucleotides (nt);
- (2) the use of the DNA microarray as defined in (1) above for *in vitro* identification and characterisation of microorganisms in a sample or in a clinical specimen, preferably for the diagnosis of bacteremia, fungemia or sepsis;
- (3) an *in vitro* method for identification and characterisation of microorganisms in a sample or in a clinical specimen comprising
  - (a) isolating the total DNA from the sample or clinical specimen and labelling the DNA with a reporter molecule, preferably a fluorochrome;
  - (b) applying the DNA thus obtained to the DNA microarray as defined in (1) above and hybridising the DNA with the gene probes of the DNA microarray; and
  - (c) detecting DNA bound to the DNA microrarray by determination of the amount of the reporter molecules bound to the array; and
- (4) a kit for detection of microorganisms in a sample or clinical specimen comprising the microarray of embodiment (1).

Brief description of the Figures

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Fig. 1: DNA microarray analyses of 58 clinical isolates, reference strains and blood cultures.

Each column shows the results of an individual hybridisation with target DNA prepared from: *S. aureus* ATCC 29213 (1), MW2 (2), clinical isolates (3-7), positive blood cultures (8-11); *P. aeruginosa* ATCC 27853 (12), clinical isolates (13-17), positive blood culture (18); *E. coli* ATCC 25922 (19), clinical isolates (20-25), positive blood cultures (26-27); *S. epidermidis* clinical isolates (28-32), positive blood cultures (33-35); clinical isolates of *S. auricularis* (36), *S. capitis* (37), *S. haemolyticus* (38), *S. hominis* (39), and *S. warneri* (40). Other Gram-negative species included a *Proteus mirabilis* positive blood culture (41), clinical isolates of *Proteus mirabilis* (42-43), *Serratia marcescens* (44-45), *Klebsiella pneumonia* (46-48), *Stenotrophomonas maltophilia* (49), *Acinetobacter baumannii* (50), *Enterobacter cloacae* (51) and *Enterobacter aerogenes* (52); other Gram-positive species included clinical isolates of *Micrococcus* spp. (53), *Enterococcus* spp. (54), *Enterococcus faecalis* (55) and *Streptococcus pneumoniae* (56) and two positive blood cultures of *S. pneumoniae* (57-58).

- (A) Hybridisation of DNA prepared from bacterial isolates, reference strains and blood cultures with *E. coli* gene probes;
- (B) hybridisation with *P. aeruginosa* gene probes;
- (C) hybridisation with S. aureus gene probes.

Grey boxes represent gene probes which hybridised with the respective target DNA, white boxes represent gene probes which showed no hybridisation with the respective target DNA.

Fig. 2: Validation of the *S. aureus* microarray of example 11. 2 μg genomic DNA from *S. aureus* strain T94 were labelled either with Cy3 or Cy5, combined and hybridised as described in Example 11. Cy3: green signal; Cy5: red signal; double-hybridisation: yellow signal.

- A) Overlay of microarray scanned using Cy3 and Cy5 filter sets;
- B) Scatterplot of normalized fluorescence intensities of individual gene probes after microarray hybridisation. The signal intensities from both channels correlate highly with each other ( $r^2 = 0.97$ ).
- Fig. 3: Specific identification of S. aureus from distantly related bacteria using the microarray of example 11.2 μg of S. aureus DNA were co-hybridised with 2 μg of pure E. coli (A) or P. aeruginosa (B) genomic DNA. Obtained hybridisation patterns are represented as bar codes, where the 140 spotted gene segments appear subsequently and are clustered in categories (NC: negative control; PC: positive control; Antibiotic Resistance Determinants; Virulence Factors and Metabolic Functions (see Tab. 6)). Positive hybridisation is indicated by a bar while negative spots are represented by an empty area. Both assays show clear S. aureus discrimination with practically no cross hybridisation between DNA from said gram negative bacteria and S. aureus selected genes, while the positive control (16S RNA sequence) reveals the good quality of hybridisation.
- Fig. 4: Specific identification of *S. aureus* from coagulase negative staphylococci using the microarray of example 11. 2 μg of *S. aureus* DNA were co-hybridised with 2 μg of *S. epidermidis* (A) or *S. saprophyticus* (B) genomic DNA. Obtained hybridisation patterns are illustrated by scanned fluorescent picture data (A: *S. aureus*: green signal; *S. epidermidis*: red signal; B: *S. aureus*: red signal; *S. saprophyticus*: green signal) and transformed in bar codes (see legend of Fig. 3). All specific *S. aureus* virulence factor genes hybridised exclusively with *S. aureus* DNA. Yellow spots showing cross-hybridisation correspond to some shared antibiotic resistance determinants and genes associated to metabolic functions.
- Fig. 5: Specificity of the S. aureus m icroarray of example 11.
  - A) Scan of microarray hybridised with 2  $\mu$ g each of genomic DNA from *S. aureus* strain T103 (Cy3, represented in green) or T100 (Cy5, represented in red), showing remarkable genotypic differences between strains.
  - B) PCR amplification of the genes from genomic DNA of *S. aureus* (strains T100 and T103) validating results of the microarray hybridisation shown in (A).
- <u>Fig. 6:</u> Identification and characterisation of *S. aureus* from positive blood culture using the microarray of example 11. 2 μg of DNA prepared from blood culture positive for *S. aureus* (strain T95) was co-hybridised with 2 μg of DNA prepared from sterile blood culture or with 2 μg of pure *S. aureus* genomic DNA for 4 hours. Positive and negative spots are transformed in a bar code scheme (see legend of Fig. 3).
  - Sterile blood culture DNA did not cross-hybridise with spotted *S. aureus* genes (A). Blood culture positive for *S. aureus* produced a fluorescent hybridisation pattern almost identical to the pattern obtained with pure *S. aureus* genomic DNA (B).

### Definitions

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[0027] In the framework of the present invention the following terms and definitions are used.

[0028] A "DNA microarray" consists of a collection of nucleic acid sequences, preferably DNA sequences, immobilized onto a solid support, such as glass, plastic or silicon chips, in a latticed pattern (forming an "array"), Each unique sequence of said sequences forms a tiny feature on the microarray called a "spot" or "capture probe". The size of these spots varies from one system to another, but is usually less than two hundred micrometers in diameter, thus up to tens of thousands of spots can be arrayed in a total area of a few square centimeters. DNA microarrays provide a means to detect and quantity large numbers of discrete nucleic sequences in parallel. In a microarray hybridisation the nucleic acids in the sample that is being analysed (called "target") are expected to form duplexes specifically with the corresponding capture probes. Occurrence or absence of duplex formation indicate the presence or absence of said target, For routine microarray analysis, said target is commonly converted to a labelled population of nucleic acids, using reporter molecules. Hybridisation of said labelled target DNA molecules from the tested samples with complementary DNA sequences affixed in specific spots on the array can thus be detected by examination for the presence of said label on the array using a microarray scanner (Müller, H.-J., Röder, T., "Der Experimentator: Microarrays, Spektrum Akademischer Verlag, Heidelberg (2004)).

[0029] "Gene probe" or "gene probe derived from..." refers to a DNA sequence present on the microarray of present invention and used as a capture probe. It is complementary to a target DNA sequence, preferably to a microbial, more preferably to a bacterial or fungal gene or gene segment. Said gene probe is prepared by any known method of DNA synthesis, and preferably prepared by cloning the respective PCR-amplified gene or gene segment into a plasmid/vector. The recombinant gene or gene segment is then amplified by PCR, isolated from the amplification mix, purified (preferably by ethanol-purification) and finally spotted onto the array.

[0030] A "clinical isolate" is a microbial, especially a fungal or bacterial strain isolated from a clinical specimen, wherein the isolation includes at least one *in vitro* propagation.

[0031] An "isolated DNA" is a DNA separated or purified from the organism it is naturally associated with or from the clinical specimen in which it occurs. This comprises biochemically or biophysically purified native DNA, recombinant DNA, chemically synthesized DNA and DNA analogues (e.g. peptide nucleic acids).

[0032] "Native" is synonymous to "naturally (occuring)".

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[0033] A "DNA segment" or "gene segment" is an isolated DNA which contains or consists of a part of the native full-length sequence of a gene which is still able to hybridize to the native sequence under stringent hybridisation conditions. Although the present invention is in the following exclusively described as relating to "DNA" sequences, it is not to be construed as being lim ited thereto. Rather, if the term "DNA" is used in connection with the gene probes or target sequences of present invention, it includes other polynucleotides (like RNA or RNA/DNA hybrids), and DNA analogues such as PNA, phosphonate backbone DNA, artificial pentose or hexose backbone DNA which is able to hybridize with native DNA etc.. Furthermore, modified bases like deoxy bases, inosine or aminoallylcytosine may be used on all DNA, RNA and PNA backbones. However, DNA itself is the preferred polynucleotide for performance of the invention.

[0034] The DNA sequences used as gene probes in present invention are either identical, substantially identical or homologous to the complementary native target sequences. In the context of present invention, when a specific DNA sequence is denominated, this encompasses not only said specific sequence, but also the sequences substantially identical or homologous thereto, i.e. its substitution mutants. "Substantially identical" means that the DNA contains mutations of up to 10% of the total number of nt in comparison with the native DNA sequence and/or has a nucleotide identity of > 90% to the corresponding native DNA segment. Said mutations are preferably single nucleotide polymorphisms or point mutations and include the mutation of not only a single but also a few (up to 10 nt, preferably up to 5 nt) consecutive nt. "Homologous" or "homologue" refers to a DNA sequence which has a sequence identity of more than 70% of the corresponding native DNA sequence and encompasses the substantially identical DNA sequences. Preferably, the sequences used as gene probes are at least substantially identical to the corresponding native DNA sequence.

[0035] Preferred gene probes of the present invention are the DNA sequences listed in the sequence protocol, their complementary sequences or their corresponding native DNA segment.

[0036] The DNA sequences used as gene probes in present invention may also be deletion or addition mutants of the corresponding native DNA segments. In case of deletion mutants, the minimum length of the DNA sequences suitable as probes in present invention is 100 nt. Preferably, the deletions take place at the 5' - and/or 3' -terminus of the native DNA segment. In case of addition mutants, the added nucleotides may sum up to a total of 90% of the nucleotide number of the native DNA segment, if added at the 5' - or 3' - terminus of the DNA sequence. Alternatively, the additions and deletions may be of one isolated nucleotide or of 2 or more consecutive nucleotides at one or more internal site(s) of the native DNA segment. Preferably, 0-30% nucleotides of the corresponding native DNA segment are added or deleted. It is most preferred that the addition or deletion mutants used as gene probes in present invention comprise one or more segment(s) of at least 100 consecutive nt each, which are derived from one gene, and/or sequences homologous (70% homology) or complementary thereto. These segments may be embedded in or fused to other DNA sequences, which will not hybridize under stringent conditions with either human or bacterial DNA or the DNA of the target microorganism. Said other DNA sequences preferably have a maximum length wich adds up with the length of the enclosed segment (s) to not more than the upper limit for the length of gene probes suitable for present invention.

**[0037]** A "positive blood culture" is an *in vitro* culture started from whole blood or blood components wherein the growth of microorganisms has been detected. Said growth is indicated by a positive growth index. The detection is preferably done by monitoring CO<sub>2</sub> production in the blood culture.

[0038] "Direct identification" of microorganisms refers to an identification method which comprises isolation of DNA from a sample or clinical specimen, but does not require an amplification of the genetic material of the microorganisms after said isolation in order to identify the microorganisms using the method of present invention. The isolated genetic material is labelled and applied to the DNA microarray of present invention without prior amplification, i.e. directly after isolation or after a short workup step.

[0039] A "detection method" in the context of the present invention is a method for determination of hybridisation of DNA molecules contained in a sample to the probes on the solid support of the microarray of present invention. This method may be any textbook method for detection of DNA hybridisation on microarrays, e.g. direct detection or labelling of target DNA with a reporter molecule and consecutive visualisation of the reporter molecule. Preferred detection methods are said labelling method and the direct detection by electrical biosensors or mass spectrometry (Liu, R. H. et al., Anal. Chem. 76(7):1824-31 (2004); Stomakhin, A. A. et al., Nucleic Acids Res. 28(5):1193-8 (2000)).

**[0040]** A "reporter molecule" in the context of the method of the present invention is a chemical or physical marker which allows differentiation of labelled from unlabelled DNA by physical, chemical or immunological methods. The labelling method includes, but is not limited to radioactive labelling (e.g. with <sup>33</sup>P, <sup>32</sup>P), fluorescent/luminescent/chromophor labelling and hapten labelling (i.e. psoralen or DIG). It is followed by an appropriate detection step necessary to

determine the presence and/or quantity of the reporter molecule, namely scintillation counting (e.g. phosphoimaging); photooptic measurement (e.g. fluorescence measurement, luminescence measurement) and antibody-based detection (including colorimetric, luminescence or fluorescence detection), respectively. Preferably, the reporter molecule is a fluorochrome/fluorophor (both terms are used as synonyms in the context of present invention) which includes but is not limited to cyanines, fluoresceins and rhodamines. More preferably, it is of the cyanine group of fluorophores. Most preferably, it is selected from the group consisting of the fluorophores Cy3, Cy5 or Alexa Fluor 647 and Alexa Fluor 546. The ratio of base to dye molecules (BDR) in DNA labelled with such reporter molecules is preferably less or equal to 60.

Detailed description of the invention

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**[0041]** The present invention provides a DNA microarray and its use for rapid identification and characterisation of microorganisms in a sample or clinical specimen (embodiments (1) to (3)).

**[0042]** The DNA microarray of embodiment (1) of the invention comprises gene specific DNA sequences as capture probes, which allow the identification of microbial species ("target species"), especially of bacterial and fungal species, and/or their further characterisation with regard to antibiotic resistance and virulence. Preferably, it allows the identification and characterisation of the target species. It is specific, applicable to the analysis of DNA isolated from blood cultures and suitable to detect resistance genes.

[0043] One important feature of the microarray of the present invention is that the panel of probes can be continually extended to include sequences for additional species, variant isolates or antibiotic resistance determinants as they are characterised and available. The accuracy, range and discriminatory power of the gene-segment based microarray can be refined by adding or removing gene probes to the panel without significantly increasing complexity or costs. In a pilot study, three important species causing bacteremia were selected to provide a proof of principle (examples 1-10). The range of organisms that can be identified can be easily expanded by increasing the number of gene probes on the array. For example, addition of a few probes specific for *S. epidermidis* and other CoNS will allow for the species identification of coagulase-negative staphylococci. Furthermore, due to a specific hybridisation pattern for each species it will also allow the identification of mixed blood cultures with more than one pathogen.

[0044] A second important feature of this microarray format is the length of the DNA sequences used as gene probes. They are at least 100 nt, preferably 100-3000 nt long. In an especially preferred aspect of embodiment (1) the length of the gene probes is from 100 to 1000 nt, most preferably from 200 to 800 nt. Thus, one probe per gene is usually sufficient to produce strong signals and high specificity (Stears, R.L. et al., Nat. Med., 9:140-5 (2003)). For long probes like these, minor point mutations are likely to only slightly reduce duplex formation, which does not lead to the loss of hybridisation signals. In contrast, short oligonucleotide microarrays sometimes lack specificity and require multiple short oligonucleotides per one gene.

**[0045]** The microorganims or microbial DNA to be detected using the microarray of present invention are preferably bacteria (such as *Staphylococci*, *Enterococci*, *Streptococci*, *E. coli*, *P. aeruginosa*) or fungi (such as yeasts and filamentous fungi, in particular *Candida* spp., *Aspergillus* spp., *Cryptococcus* spp., *Malassezia* spp., *Trichosporin* spp.), respectively bacterial or fungal DNA. The microarray is especially suitable for direct identification and characterisation of bacteria and *C. albicans*.

[0046] In one preferred aspect of embodiments (1), (2) and (3), the DNA microarray is feasible to identify and characterize any of the microorganisms, including the fungi and bacteria as defined above, known as etiological agents of fungemia, bacteremia or sepsis. In another preferred aspect of (1), it is feasible to characterize the bacteria known as etiological agents of bacteremia or sepsis. More preferably, it is feasible to identify and characterize at least 90 % of said microorganisms or bacteria. Equally more preferably it is feasible to identify and characterize microorganisms selected from the group consisting of *S. aureus, Coagulase-negative staphylococci, Enterococci, Streptococci, E. coli, Klebsiella* spp., *Proteus* spp., *Enterobacter* spp., *P. aeruginosa, Stenotrophomonas* spp., *Acinetobacter* spp. and *Candida albicans*, most preferably microorganisms selected from the group consisting of *C. albicans, Enterococcus faecalis, Enterococcus faecium, E. coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Enterobacter cloacae, <i>P. aeruginosa, Stenotrophomonas maltophilia, Acinetobacter baumannii, S. aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus lugdunensis, Staphylococcus warneri, Streptococcus agalactiae, Streptococcus bovis, Streptococcus dysgalactiae, Streptococcus mitis, Streptococcus mutans, Streptococcus pneumoniae, Streptococcus pyogenes. Most preferably, it is feasible to identify and characterize at least <i>S. aureus, E. coli* and *P. aeruginosa*.

[0047] The practicability and specificity of the DNA microarray for the identification and characterisation of *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* grown in blood culture specimens was evaluated with clinical isolates and positive blood cultures (Examples 1-10). Especially preferred is a microarray which allows identification and characterisation of *S. aureus*. The latter microarray allows the detection of every *S. aureus* isolate, unambiguously identifies most of important virulence genes such as *tsst-1*, *sea*, *seb*, *eta* and antibiotic resistance genes such as *mecA*, *aacA-aphD*, *blaZ*, *ermA* and specifically distinguishes *S. aureus* from unrelated gram negative bacteria, e.g.

Escherichia coli or Pseudomonas aeruginosa, as well as from closely related CoNS (Example 11, Fig. 2-6).

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[0048] In another preferred aspect of the invention, the microarray of (1) is suitable for diagnosis of fungemia, bacteremia or sepsis; especially for diagnosis of bacteremia, candidemia, and bacterial or *Candida* sepsis.

[0049] The present invention provides a novel approach for detection of microorganisms, especially of bacteria and fungi, by microarrays: using gene-segments it allows species identification by probing a large and diverse set of species-specific genes. Such an approach is reliable since it makes possible to identify a pathogen even when some genes have been deleted from its genome. Furthermore, the selected DNA probes are at least 100 nt, preferably 200 to 800 nt long and are therefore not sensitive to single nucleotide polymorphisms or CG-content variations in the targets. Therefore, a gene segment array according to present invention is useful for indicating the presence of a gene even though the sequence may be slightly altered e.g. by point mutations (Southern, E. et al., Nat. Genet. 21 :5-9 (1999)). Additionally, it permits species virulence and antibiotics resistance profiling all together in a single-step test. Thus, present invention provides for a significant improvement compared to the classical approach focused on the detection of a short evolutionary conserved sequence like 16S RNA.

[0050] The number and perfect composition of gene-segments necessary for a correct species identification, virulence determination and resistance profiling must be determined by empiric specificity tests. Thus, in a preferred aspect of the invention, the DNA microarray of embodiment (1) comprises the minimal number of species specific gene probes which is sufficient for species identification, the minimal number of virulence gene probes which is sufficient for virulence determination, and/or the minimal number of resistance gene probes which is sufficient for determination of resistance of a specific microorganism. Preferably, the minimal number of gene probes in this aspect of the invention is: for correct species identification at least 2 different species specific gene probes per target species, more preferably at least 10, most preferably at least 20; for virulence determination at least 1 gene probe per target species, more preferably at least 5 different gene probes, even more preferably at least 20 different gene probes, most preferably gene probes for all known virulence factors of each target species; for determination of resistance at least 1 gene probe per antibiotic class or resistance factor, more preferably at least 5 different gene probes, most preferably all known gene-coded resistance determinants in the target species.

[0051] Generally, the DNA microarray of embodiment (1) comprises gene probes which are specific for a microbial species, bacterial/fungal species or a group of microorganisms to be identified. Said gene probes are preferably DNA sequences selected from three different groups, namely (a) species specific gene probes; (b) virulence gene probes; and/or (c) resistance gene probes. Preferably, the species specific set of gene probes for each species to be identified and characterised is selected from species specific gene probes (a) for

- (i) Staphylococcus aureus including gene probes derived from cataSaur, clfA, clfB, coa, I-clpC, I-clpP, I-ctaA, I-ctsR, I-dltA, I-dltB, I-dltC, I-dnaK, I-elkT, I-femD, I-glnA, I-glnA, I-grlA, I-grlB, I-groEL, I-groES, I-hemA, I-hemE, I-hemH, I-hemL, I-hemY, I-lepA, I-IrgA, I-IrgB, I-lytM, I-menB, I-menD, I-menE, I-menF, I-mreB, I-mreR, I-mutL, I-mutS, I-NAG, I-pbg, I-pbpF, I-pdhB, I-pdhC, I-rsbU, I-rsbV, I-rsbW, I-sgp, I-sirR, I-sodA, I-sodB, I-sstA, I-sstB, I-sstC, I-sstD, I-trx, I-yhiN, epiP-bsaP, geh, gyrA, gyrB, hemB, hemC, hemD, hemN, hsdS, hsdS, lip, menC, nuc, pdhD, rpoB, SAV0431, SAV0439, SAV0440, SAV0441, sigB, spa, sstC, tag, tyrA, I-aroC, I-aroA, I-cna, I-ebpS, I-eno, I-fbpA, I-fib, I-fnbB, I-srtA, I-stpC, I-fnbA, I-spa, I-aroE, I-aroF, I-aroG, I-asp23, I-atl;
- (ii) Escherichia coli including gene probes derived from b1169, envZ, fliCb, nfrB, nlpA, pilAe, yacH, yagX, ycdS, yciQ, ymcA;
- (iii) Staphylococcus epidermidis including gene probes derived from ardeSE0106, ardeSE0107, aroiSE0105, atlE, agrB, agrC, alphSE1368, gad, glucSE1191, hsp10, icaA, icaB, m vaSSepid, nitreSE1972, nitreSE1974, nitreSE1975, oiamtSE1209, ORF1Sepid, ORF3bSepid, qacR, sin, ureSE1861, ureSE1863, ureSE1864, ureSE1865, ureSE1867;
- (iv) Staphylococcus haemolyticus including gene probes derived from folQShaemolyt, mvaCShaemolyticus, mvaD-Shaemolyt, mvaK1Shaemolyticus, mvaSShaemolyticus, RNApolsigm;
- (v) Staphylococcus lugdunensis including gene probes derived from agrB2Stalugd, agrC2Stalugd, agrCStalugd, slamStalugd;
- (vi) Staphylococcus warneri including gene probes derived from msrw1Stwar, nukMStwar, proDStwar, proMStwar, sigrpoStwar, tnpStwar;
- (vii) Candida albicans including gene probes derived from ARG56, ASL43f, BGL2, CACHS3, CCT8, CDC37, CEF3, CHS1, CHS2, CHS4, CHS5, CHT1, CHT2, CHT4, CSA1, 5triphosphatase, AAF1, ADH1, ALS1, ALS7, EDT1, ELF, ESS1, FAL1, GAP1, GNA1, GSC1, GSL1, HIS1, HTS1, HWP1, HYR1, INT1a, KRE15f, KRE6, KRE9, MIG1, MLS1, MP65, NDE1, PFK2, PHR1, PHR2, PHR3, PRA1, PRS1, RBT1, RBT4, RHO1, RNR1, RPB7, RPL13, RVS167, SHA3, SKN1, SRB1, TCA1, TRP1, YAE1, YRB1, YST1exon2;
- (viii) Enterococcus faecalis including gene probes derived from arcA, arcC, bkdA, cad, camE1, csrA, dacA, dfr, dhoD1a, ABC-eltA, agrBfs, agrCfs, dnaE, ebsA, ebsB, eep, efaR, gls24\_glsB, gph, gyrAEf, metEf, mntHCb2, mob2, mvaD, mvaE, parC, pcfG, phoZ, polC, ptb, recS1, rpoN, tms, tyrDC, tyrs;

- (ix) Enterococcus faecium including gene probes derived from bglB, bglR, bglS, efmA, efmB, efmC, mreC, mreD, mvaDEfaecium, mvaEEfaecium, mvaK1Efaecium, m vaK2Efaecium, m vaSEfaecium, orf3\_4Efaeciumb, orf6\_7Efaecium, orf7\_8Efaecium, orf9\_10Efaecium;
- (x) Klebsiella pneumonia including gene probes derived from atsA, atsB, budC, citA, citW, citX, dalD, dalK, dalT, acoA, acoB, acoC, ahlK, fimK, glfKPN2, ltrA, mdcC, mdcF, mdcH, mrkA, mtrK, nifF, nifK, nifN, tyrP, ureA, wbbO, wza, wzb, wzmKPN2, wztKPN2, yojH, liac;

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wzy6bStrpneum, xpt;

- (xi) Klebsiella oxytoca including gene probes derived from cymA, cymD, cymE, cymH, cymI, cymJ, ddrA, fdt-1, fdt-2, fdt-3, gatY, hydH, masA, nasA, nasE, nasF, pehX, pelX, tagH, tagH, tagF;
- (xii) Pseudomonas aeruginosa including gene probes derived from glpR, lasRb, OrfX, pa0260, pa0572, pa0625, pa0636, pa1046, pa1069, pa1846, pa3866, pa4082, pilAp, PilAp2, pilC, PstP, purK, uvrDII, vsml, vsmR, xcpX; (xiii) Streptococcus pneumoniae including gene probes derived from cap1EStrpneu, cap1FStrpneu, cap1GStrpneu, cap3AStrpneu, cap3BStrpneu, celAStrpneu, celBStrpneu, cglAStrpneu, cglBStrpneu, cglCStrpneu, cglDStrpneu, cinA, cps14EStrpneum, cps14FStrpneum, cps14GStrpneum, cps14HStrpneum, cps19aHStrpneum, cps19aHStrpneum, cps19aHStrpneum, cps19alStrpneum, cps19aKStrpneum, cps19fGStrpneum, cps23fGStrpneum, dexB, dinF, 1760Strpneu, acyPStrpneu, endAStrpneu, exoAStrpneu, exp72, fnlAStrpneu, fnlBStrpneu, fnlCStrpneu, gct18Strpneum, hexB1, hftsHstrpneu, immunofrag1Strpneu, immunofrag2Strpneu, immunofrag3Strpneu, KdtBStrpneu, lyAStrpneu, pcpBStrpneu, pflCStrpneu, plpA, prtA1Strpneu, pspC1Strpneu, pspC2, purRStrpneu, pyrDAStrpneum, SP0828Strpneu, SP0830Strpneu, SP0833Strpneu, SP0837\_38Strpneu, SP0839Strpneu, ugdStrpneum, wciO6bStrpneum, wci
- (xiv) Streptococcus agalactiae including gene probes derived from cpsA1Strgal, cpsB1Strgal, cpsC1Strgal, cpsD1Strgal, cpsE1Strgal, cpsG1Strgal, cpsIStragal, cpsIStragal, cpsKStragal, cpsMStragal, cpsYStragal, cpsIStragal, cpsKStragal, cpsMStragal, cpsYStragal, cylBStraga, cylEStraga, cylFStraga, cylHStraga, cylIStraga, cylIStraga, cylKStraga, 0487Straga, 0498Straga, 0500Straga, 0502Straga, 0504Straga, folDStraga, neuA1Strgal, neuB1Strgal, neuC1Strgal, neuD1Strgal, recNStraga, ileSStraga;

wciP6bStrpneum, wciY18Strpneum, wzdbStrpneum, wze6bStrpneum, wzy18Strpneum, wzy4Strpneum,

- (xv) Streptococcus pyogenes including gene probes derived from cyclStrpyog, fah\_rph\_hlo\_Strpyog, int, int315.5, murEStrpyog, oppA, oppCStrpyog, oppD, SPy0382Strpyog, SPy0390Strpyog, SpyM3\_1351, vicXStrpyog;
- (xvi) Streptococcus viridans including gene probes derived from 573Stprmut, 580SStprmut, 581\_582SStprmut, 584SStprmut, dltAStrmut, dltBStrmut, dltCppx1Strmut, dltDStrmut, lichStrbov, lytRStprmut, lytSStprmut, pepQStrrmut, pflCStrmut, recNStprmut, ytqBStrmut;
- (xvii) Proteus mirabilis including gene probes derived from atfA, atfB, atfC, ccmPrmi1, cyaPrmi, aad, flfB, flfD, flfN, flhD, floA, ftsK, gstB, hemCPrmi, hemDPrmi, hev, katA, lpp1, menE, mfd, nrpA, nrpB, nrpG, nrpS, nrpT, nrpU, pat, pmfA, pmfC, pmfE, ppaA, rsbA, rsbC, speB, stmA, stmB, terA, terD, umoA, umoB, umoC, ureR, xerC, ygbA; (xviii) Proteus vulgaris including gene probes derived from envZPrvu, frdC, frdD, infBPrvu, lad, tna2.

[0052] Preferably, the virulence specific set of gene probes for each species to be identified and characterised is selected from virulence gene probes (b) for

- (i) Staphylococcus aureus including gene probes derived from bsaE, bsaG, cap5h, cap5i, cap5k, cap8H, cap8I, cap8J, cap8K, I-hId, I-hysA, I-IgGbg, EDIN, eta, etb, hglA, hglB, hglC, hla, hlb, lukF, lukS, NAG, sak, sea, seb, sec1, seg, seh, sel, set15, set6, set7, set8, sprV8, tst, I-sdrC, I-sdrD, I-sdrE;
  - (ii) Escherichia coli including gene probes derived from b1202, eae, eltB, escR, escT, escU, espB, fes, fteA, hlyA, hlyB, iucA, iucB, iucC, papG, rfbE, shuA, SLTII, toxA-LTPA, VT2vaB;
- (iii) Staphylococcus epidermidis including gene probes derived from gcaD, hld\_orf5, icaC, icaD, icaR, psm\_ beta1and2, purR, spoVG, yabJ;
  - (iv) Staphylococcus haemolyticus including gene probes derived from lipShaemolyt;
  - (v) Staphylococcus lugdunensis including gene probes derived from fblStalugd, slushABCStalugd;
  - (vi) Staphylococcus warneri including gene probes derived from gehAStwar;
  - (vii) Candida albicans including gene probes derived from CCN1, CDC28, CLN2, CPH1, CYB1, EFG1, MNT1, RBF1, RBF1, RIM101, RIM8, SEC14, SEC4, TUP1, YPT1, ZNF1 CZF1;
    - (viii) Enterococcus faecalis including gene probes derived from asa1, asp1, cgh, cylA, cylB, cyll, cylL\_cylS, cylM, ace, ef00108, ef00109, ef0011, ef00113, ef0012, ef0022, ef0031, ef0032, ef0040, ef0058, enlA, esa, esp, gelE, groEL, groES, rt1, sala, salb, sea1, sep1, vicK, yycH, yycl, yycJ;
    - (ix) Enterococcus faecium including gene probes derived from entA\_entl, entD, entR, oep, sagA;
      - (x) Klebsiella pneumonia including gene probes derived from cim, aldA, hemly, pSL017, pSL020, rcsA, rmlC, rmlD, waaG, wbbD, wbbM, wbbN, wbdA, wbdC, wztKpn, yibD;
      - (xi) P. aeruginosa including gene probes derived from aprA, aprE, ctx, algB, algN, algR, ExoS, fpvA, lasRa, lipA,

- lipH, Orf159, Orf252, pchG, PhzA, PhzB, PLC, plcN, plcR, pvdD, pvdF, pyocinS1, pyocinS1im, pyocinS2, pys2, rbf303, rhlA, rhlB, rhlR, TnAP41, toxA;
- (xii) Streptococcus pneumoniae including gene probes derived from igaStrpneu, lytA, nanA, nanBStrpneu, pcpC-Strpneu, ply, prtAStrpneu, pspA, SP0834Strpneu, sphtraStrpneu, wciJStrpneu, wziyStrpneu, wzxStrpneu;
- (xiii) Streptococcus agalactiae including gene probes derived from CAMPfactor, 0499Straga, hylStragal, lipStragal; (xiv) Streptococcus pyogenes including gene probes derived from DNaselStrpyog, fba2Strpyog, fhuAStrpyog, fhuB1Strpyog, fhuDStrpyog, hylA, hylP, hylp2, oppB, ropB, scpAStrpyog, sloStrpyog, smez-Strpyog, sof, speA, speB2Strpyog, speCStrpyog, speJStrpyog, srtBStrpyog, srtCStrpyog, srtEStrpyog, srtFStrpyog, srtGStrpyog, srtKStrpyog, srtRStrpyog, srtTStrpyog, vicKStrpyog;
- (xvi) Streptococcus viridans including gene probes derived from hlyXStrmut, igaStrmitis, igaStrsanguis, perMStrmut; (xvii) Proteus mirabilis including gene probes derived from flaA, laD, fliA, hpmA, hpmB, lpsPrmi, mrpA, mrpB, mrpD, mrpD, mrpE, mrpF, mrpG, mrpH, mrpI, mrpJ, patA, putA, uca, ureDPrmi, ureEPrmi, ureFPrmi, zapA, zapB, zapD, zapE.
- 15 [0053] Preferably, the resistance specific set of gene probes is selected from resistance gene probes (c) derived from genes coding for
  - (i) beta-lactams resistance including gene probes derived from blalMP-7, meclSepid, blaOXA-10, blaB, ampC, I-blaR, blaOXA-32, bla-CTX-M-22, pbp2aStrpneu, blaSHV-1, blaOXA-2, blaRShaemolyt, blalMP-7, I-mecR, blaOXY, dacCStrpyog, femA, mecA, blalShaemolyt, blavim, pbp2b, pbp2prim eSepid, pbp2x, pbp3Saureuc, pbp4, pbp5Efaecium, pbpC, I-mecl, pbp1a, I-blal, blaTEM-106, blaOXY-KLOX, ftsWEF, fmhB, cumA, femBShaemolyt, blaPER-1, bla\_FOX-3, blaA, psrb, fmhA, mecR1Sepid, blaZ, blaOXA-1, fox-6, blaPrmi;
  - (ii) aminoglycosides resistance including gene probes derived from aacA\_aphDStwar, aacC1, aacC2, strB, aadA, aadB, aadD, aacA4, strA, aph-A3, aacC1, aacA4, aacA-aphD, I-spc, aphA3;
  - (iii) macrolides-lincosamines-streptogramins resistance including gene probes derived from ermC, linB, satSA, mdrSA, I-linA, ermB, ermA, satA, msrA, mphBM, mefA, mrx;
  - (iv) trim ethoprim resistance including gene probes derived from dfrA, dfrStrpneu;
  - (v) chloramphenicol resistance including gene probes derived from cat, catEfaecium, cmlA5;
  - (vi) tetracyclines resistance including gene probes derived from tetAJ, tetL, tetM
  - (vii) glycopeptides resistance including gene probes derived from vanH(tn), vanA, vanHB2, vanR, vanRB2, vanS (tn), vanSB2, vanVIIB2, ddl, ble, vanXB2, vanY(tn), vanYB2, vanB, vanZ(tn), vanC-2, vanX(tn);
    - (viii) multiple target resistance including gene probes derived from acrB, m exB, I-qacA, sull, sul, cadBStalugd, mexA, acrR, emeA, acrA, rtn, abcXStrpmut, qacEdelta1, elkT-abcA, 1-cadA, albA, wzm, msrCb, nov, wzt, wbbl, norA23, mexR, arr2, mreA, I-cadC, uvrA;
  - (ix) fungicides resistance, especially *C. albicans* fungicide resistance, including gene probes derived from *CRD2*, *CDR1*, *MET3*, *FET3*, *FTR2*, *MDR1-7*, *ERG11*, *SEC20*.
  - [0054] Furthermore, the microarray may contain a set of gene probes which serve as controls. Preferably, such a set of control gene probes is selected from group (d) consisting of control gene probes coding for
    - (i) negative controls, namely DNA sequences which will not hybridise with human DNA or bacterial, fungal or the microbial target DNA under the hybridisation conditions of the method of present invention, including gene probes derived neither from fungal, bacterial or target microbial nor from human genes, preferably gene probes derived from plant genes, more preferably from *Arabidopsis thaliana* or *Glycine max* genes;
    - (ii) positive controls including segments of ribosomal DNA from bacterial target species, preferably 16S DNA, and segments of conserved human genes;
    - (iii) positive controls specific for DNA added to the sample ("spiked DNA"), namely DNA sequences which will not hybridise with human DNA or the fungal, bacterial or microbial target DNA under the hybridisation conditions of the method of present invention, including gene probes derived neither from fungal, bacterial or target microbial nor from human genes, preferably gene probes derived from mouse or amoeba genes, most preferably from *Mus musculus* or *Dictyostelium discoideum* genes.

[0055] These control gene probes are necessary to

a) detect non-specific hybridisation;

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- b) optimise hybridisation conditions and image acquisition and analysis;
- c) provide positive controls for the quality of probe preparation, hybridisation and detection; and/or
- d) control technical aspects of the entire detection procedure including labelling, hybridisation and detection steps.

**[0056]** In a preferred aspect of embodiment (1), the microarray contains DNA sequences selected from the group consisting of the SEQ ID NOs: 1-918, complementary sequences thereto, addition mutants, deletion mutants, substitution mutants and homologues thereof as gene probes.

[0057] More preferably, in order to identify a specific microbial species, bacterial species or group of bacteria, the gene probes of group (a) are selected from SEQ ID NO: 1-99, 142-152, 174-199, 209-214, 216-219, 222-229, 231-291, 308-342, 377-393, 399-431, 449-490, 523-591, 606-639, 645-656, 687-701, 706-749 and 776-781 (compare Tab. 1). Equally, in order to determine virulence of a specific microorganism or bacterial species, the gene probes of group (b) are selected from SEQ ID NO: 100-141, 153-173, 200-208, 215, 220-221, 230, 292-307, 343-376, 394-398, 432-448, 491-522, 592-605, 640-644, 657-686, 702-705, 750-775 and 782-784 (compare Tab. 1). Equally, in order to determine antibiotic resistance of a specific microbial or bacterial species, the gene probes of group (c) are selected from SEQ ID NO:785-918, preferably from SEQ ID NO:785-882 (compare Tab. 1). Equally, in order to provide the required controls (negative, positive, hybridisation controls), the gene probes of group (d) are selected from SEQ ID NO:919-947, preferably from SEQ ID NO:919-925 and 944-947, more preferably from SEQ ID NO: 919 and 921 (compare Tab. 1).

[0058] <u>Tab. 1:</u> Preferred gene probes for species identification, virulence determination and resistance determination of microorganisms

a) probes for species identification

SEQ ID NO	Probe	
Staphylococcus aureus identification		
1	cataSaur_1_1	
2	cataSaur_1_2	
3	clfA_1_1	
4	clfB_1_1	
5	coa_1_1	
6	coa_1_2	
7	I-clpC_1_1	
8	I-clpP_1_1	
9	I-ctaA_1_1	
10	I-ctsR_1_1	
11	l-dltA_1_1	
12	I-dltB_1_1	
13	I-dltC_1_1	
14	l-dnaK_1_1	
15	l-elkT_1_1	
16	I-femD_1_1	
17	l-glnA_1_1	
18	l-glnR_1_1	
19	I-qrIA_1_1	
20	I-grlB_1_1	
21	l-groEL_1_1	
22	I-groES_1_1	
23	I-hemA_1_1	
24	I-hemE_1_1	
25	I-hemH_1_1	
26	I-hemL_1_1	

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	SEQ ID NO	Probe
5	Staphylococcus aureus identification	
	27	I-hemY_1_1
	28	I-lepA_1_1
	29	I-lrgA_1_1
10	30	I-IrgB_1_1
	31	I-lytM_1_1
	32	I-menB_1_1
15	33	I-menD_1_1
	34	I-menE_1_1
	35	I-menF_1_1
	36	I-mreB_1_1
20	37	I-mreR_1_1
	38	l-mutL_1_1
	39	I-mutS_1_1
25	40	I-NAG_1_1
	41	l-pbg_1_1
	42	I-pbpF_1_1
	43	I-pdhB_1_1
30	44	I-pdhC_1_1
	45	I-rsbU_1_1
	46	I-rsbV_1_1
35	47	I-rsbW_1_1
	48	I-sgp_1_1
	49	I-sirR_1_1
	50	I-sodA_1_1
40	51	I-sodB_1_1
	52	I-sstA_1_1
	53	I-sstB_1_1
45	54	I-sstC_1_1
	55	I-sstD_1_1
	56	I-trx_1_1
50	57	l-yhiN_1_1
	58	epiP-bsaP_1_1
	59	geh_1_1
	60	gyrA_1_1
55	61	gyrB_1_1
	62	hemB_1_1
	63	hemC_1_1

	SEQ ID NO	Probe
5	Staphylococcus aureus identification	
	64	hemD_1_1
	65	hemN_1_1
	66	hsdS_1_1
10	67	hsdS_2_1
	68	lip_1_1
	69	menC_1_1
15	70	murC_1_1
	71	nuc_1_1
	72	pdhD_1_1
	73	rpoB_1_1
20	74	SAV0431_1_1
	75	SAV0439_1_1
	76	SAV0440_1_1
25	77	SAV0441_1_1
	78	sigB_1_1
	79	spa_1_2
	80	sstC_1_1
30	81	tag_1_1
	82	tyrA_1_1
	83	I-aroC_1_1
35	84	l-aroA_1_1
	85	I-cna_1_1
	86	I-ebpS_1_1
	87	l-eno_1_1
40	88	I-fbpA_1_1
	89	I-fib_1_1
	90	I-fnbB_1_1
45	91	l-srtA_1_1
	92	I-stpC_1 _1
50	93	I-fnbA_1 _1
	94	I-spa_1_1
	95	I-aroE_1_1
	96	I-aroF_1_1
55	97	I-aroG_1_1
	98	I-asp23_1_1
	99	l-atl_1_1

	Escherichia coli identification		
5	142	b1169_1_1	
	143	envZ_1_1	
	144	fliCb_1_1	
	145	nfrB_1_1	
10	146	nlpA_1_1	
	147	pilAe_1_1	
	148	yacH_1_1	
15	149	yagX_1_1	
	150	ycdS_1_1	
	151	yciQ_1_1	
	152	ymcA_1_1	
20	Staphylococcus	epidermidis identification	
	174	ardeSE0106_1_1	
	175	ardeSE0107_1_1	
25	176	aroiSE0105_1_1	
	177	atIE_1_1	
	178	agrB_1_1	
	179	agrC_1_1	
30	180	alphSE1368_1_1	
	181	gad_1_1	
	182	glucSE1191_1_1	
35	183	hspl0_1_1	
	184	icaA_1_1	
	185	icaB_1_1	
	186	mvaSSepid_1_1	
40	187	nitreSE1972_1_1	
	188	nitreSE1974_1_1	
	189	nitreSE1975_1_1	
45	190	oiamtSE1209_1_1	
	191	ORF1Sepid_1_1	
50	192	ORF3bSepid_1_1	
	193	qacR_1_1	
	194	sin_1_1	
	195	ureSE1861_1_1	
55	196	ureSE1863_1_1	
	197	ureSE1864_1_1	
	198	ureSE1865_1_1	

## (continued)

5	Staphylococcus	epidermidis identification
	199	ureSE1867_1_1
	Staphylococcus haemolyticus identification	
	209	folQShaemolyt_1_1
	210	mvaCShaemolyticus_1_1
10	211	mvaDShaemolyt_1_1
	212	mvaK1 Shaemolyticus_1_1
	213	mvaSShaemolyticus_1_1
15	214	RNApolsigm_1_1
	Staphylococcus	<i>lugdunensis</i> identification
	216	agrB2Stalugd_1_1
	217	agrC2Stalugd_1_1
20	218	agrCStalugd_1_1
	219	slamStalugd_1_1
	Staphylococcus	saprophyticus identification
25	222	RNApolsigmSsapro_1_1
	223	RNApolsigmSsapro_1_2
	Staphylococcus warneri identification	
	224	msrw1Stwar_1_1
30	225	nukMStwar_1_1
	226	proDStwar_1_1
	227	proMStwar_1_1
35	228	sigrpoStwar_1_1
	229	tnpStwar_1_1
	Candida albicans identification	
	231	ARG56_1_1
40	232	ASL43f_1_1
	233	BGL2_1_1
	234	CACHS3_1_1
45	235	CCT8_1_1
	236	CDC37_1_1
	237	CEF3_1_1
	238	CHS1_1_1
50	239	CHS2_1_1
L		

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Candida albicans	s identification
240	CHS4_1_1
241	CHS5_1_1
242	CHT1_1_1
243	CHT2_1_1
244	CHT4_1_1
245	CSA1_1_1
246	5triphosphatase_1_1
247	AAF1_1_1
248	ADH1_1_1
249	ALS1_1_1
250	ALS7_1_1
251	EDT1_1_1
252	ELF_1_1
253	ESS1_1_1
254	FAL1_1_1
255	GAP1_1_1
256	GNA1_1_1
257	GSC1_1_1
258	GSL1_1_1
259	HIS1_1_1
260	HTS1_1_1
261	HWP1_2_1
262	HYR1_1_1
263	INT1a_1_1
264	KRE15f_1_1
265	KRE6_1_1
266	KRE9_1_1
267	MIG1_1_1
268	MLS_1_1
269	MP65_1_1
270	NDE1_1_1
271	PFK2_1_1
272	PHR1_1_1
273	PHR2_1_1
274	PHR3_1_1
275	PRA1_1_1
276	PRS_1_1
277	RBT1_1_1
	240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276

	Candida albicans identification	
5	278	RBT4_1_1
	279	RHO1_1_1
	280	RNR1_1_1
	281	RPB7_1_1
10	282	RPL13_1_1
	283	RVS167_1_1
	284	SHA3_1_1
15	285	SKN1_1_1
	286	SRB1_1_1
	287	TCA1_1_1
	288	TRP1_1_1
20	289	YAE1_1_1
	290	YRB1_1_1
	291	YST1exon2_1_1
25	Enterococcus fac	ecalis identification
	308	arcA_1_1
	309	arcC_1_1
	310	bkdA_1_1
30	311	cad_1_1
	312	camE1_1_1
	313	csrA_1_1
35	314	dacA_1_1
	315	dfr_1_1
	316	dhoD1a_1_1
	317	ABC-eltA_1_1
40	318	agrBfs_1_1
	319	agrCfs_1_1
	320	dnaE_1_1
45	321	ebsA_1_1
	322	ebsB_1_1
	323	eep_1_1
50	324	efaR_1_1
	325	gls24_glsB_1_1
	326	gph_1_1
55	327	gyrAEf_1_1
	328	metEf_1_1
	329	mntHCb2_1_1

	Enterococcus faecalis identification		
5	330	mob2_1_1	
	331	mvaD_1_1	
	332	mvaE_1_1	
	333	parC_1_1	
10	334	pcfG_1_1	
	335	phoZ_1_1	
	336	polC_1_1	
<i>15</i>	337	ptb_1_1	
	338	recS1_1_1	
	339	rpoN_1_1	
	340	tms_1_1	
20	341	tyrDC_1_1	
	342	tyrS_1_1	
	Enterococcus fac	ecium identification	
25	377	bglB_1_1	
	378	bgIR_1_1	
	379	bglS_1_1	
	380	efmA_1_1	
30	381	efmB_1_1	
	382	efmC_1_1	
	383	mreC_1_1	
<i>35</i>	384	mreD_1_1	
	385	mvaDEfaecium_1_1	
	386	mvaEEfaecium_1_1	
	387	mvaK1Efaecium_1_1	
40	388	mvaK2Efaecium_1_1	
	389	mvaSEfaecium_1_1	
	390	orf3_4Efaeciumb_1_1	
45	391	orf6_7Efaecium_1_1	
	392	orf7_8Efaecium_1_1	
	393	orf9_10Efaecium_1_1	
	Klebsiella pneumoniae identification		
50	399	atsA_1_1	
	400	atsB_1_1	
	401	budC_1_1	
55	402	citA_1_1	
·			

	Klebsiella pneumoniae identification		
5	403	citW_1_1	
	404	citX_1_1	
	405	daID_1_1	
	406	dalK_1_1	
10	407	daIT_1 _1	
	408	acoA_1_1	
	409	acoB_1_1	
15	410	acoC_1_1	
	411	ahlK_1_1	
	412	fimK_1_1	
	413	glfKPN2_1_1	
20	414	ltrA_1_1	
	415	mdcC_1_1	
	416	mdcF_1_1	
25	417	mdcH_1_1	
	418	mrkA_1_1	
	419	mtrK_1_1	
	420	nifF_1_1	
30	421	nifK_1_1	
	422	nifN_1_1	
	423	tyrP_1_1	
35	424	ureA_1_1	
	425	wbbO_1_1	
	426	wza_1_1	
	427	wzb_1_1	
40	428	wzmKPN2_1_1	
	429	wztKPN2_1_1	
	430	yojH_1_1	
45	431	liac_1_1	
	Klebsiella oxytoca identification		
	449	cymA_1_1	
50	450	cymD_1_1	
	451	cymE_1_1	
	452	cymH_1_1	
	453	cyml_1_1	
55	454	cymJ_1_1	
	455	ddrA_1_1	

	Klebsiella oxytoca identification	
-	456	fdt-1_1_1
5	457	fdt-2_1_1
	458	fdt-3_1_1
	459	gatY_1_1
10	460	hydH_1_1
	461	masA_1_1
	462	nasA_1_1
15	463	nasE_1_1
15	464	nasF_1_1
	465	pehX_1_1
	466	pelX_1_1
20	467	tagH_1_1
	468	tagK_1_1
	469	tagT_1_1
25	Pseudomonas a	eruginosa identification
	470	glpR_1_1
	471	lasRb_1_1
	472	OrfX_1_1
30	473	pa0260_1_1
	474	pa0572_1_1
	475	pa0625_1_1
35	476	pa0636_1_1
	477	pa1046_1_1
	478	pa1069_1_1
	479	pa1846_1_1
40	480	pa3866_1_1
	481	pa4082_1_1
	482	pilAp_1_1
45	483	PilAp2_1_1
	484	pilC_1_1
	485	PstP_1_1
	486	purK_1_1
50	487	uvrDII_1_1
	488	vsml_1_1
	489	vsmR_1_2
55	490	xcpX_1_1
	Streptococcus pneumoniae identification	
	523	cap1EStrpneu_1_1

		(
	Streptococcus pi	neumoniae identification
5	524	cap1FStrpneu_1_1
	525	cap1GStrpneu_1_1
	526	cap3AStrpneu_1_1
	527	cap3BStrpneu_1_1
10	528	celAStrpneu_1_1
	529	celBStrpneu_1_1
	530	cglAStrpneu_1_1
	531	cglBStrpneu_1_1
15	532	cglCStrpneu_1_1
	533	cgIDStrpneu_1_1
	534	cinA_1_1
20	535	cps14EStrpneum_1_1
	536	cps14FStrpneum_1_1
	537	cps14GStrpneum_1_1
	538	cps14HStrpneum_1_1
25	539	cps19aHStrpneum_1_1
	540	cps19alStrpneum_1_1
	541	cps19aKStrpneum_1_1
30	542	cps19fGStrpneum_1_1
	543	cps23fGStrpneum_1_1
	544	dexB_1_1
35	545	dinF_1_1
35	546	1760Strpneu_1_1
	547	acyPStrpneu_1_1
	548	endAStrpneu_1_1
40	549	exoAStrpneu_1_1
	550	exp72_1_1
	551	fnlAStrpneu_1_1
45	552	fnlBStrpneu_1_1
	553	fnlCStrpneu_1_1
	554	gct18Strpneum_1_1
50	555	hexB1_1_1
	556	hftsHstrpneu_1_1
	557	immunofrag1Strpneu_1_1
	558	immunofrag2Strpneu_2_1
55	559	immunofraq3Strpneu_2_1
55	560	kdtBStrpneu_1_1
	561	lysAStrpneu_1_1

		(
	Streptococcus pneumoniae identification	
5	562	pcpBStrpneu_1_1
	563	pflCStrpneu_1_1
	564	plpA_1_1
	565	prtA1Strpneu_1_1
10	566	pspC1Strpneu_1_1
	567	pspC2_1_1
	568	purRStrpneu_1_1
	569	pyrDAStrpneum_1_1
15	570	SP0828Strpneu_1_1
	571	SP0830Strpneu_1_1
	572	SP0833Strpneu_1_1
20	573	SP0837_38Strpneu_1_1
	574	SP0839Strpneu_1_1
	575	ugdStrpneu_1_1
	576	uncC_1_1
25	577	vicXStrepneu_1_1
	578	wchA6bStrpneum_1_1
	579	wci4Strpneum_1_1
30	580	wciK4Strpneum_1_1
	581	wciL4Strpneum_1_1
	582	wciN6bStrpneum_1_1
35	583	wciO6bStrpneum_1_1
35	584	wciP6bStrpneum_1_1
	585	wciY18Strpneum_1_1
	586	wzdbStrpneum_1_1
40	587	wze6bStrpneum_1_1
	588	wzy18Strpneum_1_1
	589	wzy4Strpneum_1_1
45	590	wzy6bStrpneum_1_1
45	591	xpt_1_1
	Streptococcus agalactiae identification	
	606	cpsA1Strqal_1_1
50	607	cpsB1Strgal_1_1
	608	cpsC1Strgal_1_1
	609	cpsD1Strgal_1_1
55	610	cpsE1Strgal_1_1
	611	cpsG1Strgal_1_1
	612	cpslStragal_1_1

		(
	Streptococcus ag	galactiae identification
5	613	cpsJStragal_1_1
	614	cpsKStraqal_1_1
	615	cpsMStragal_1_1
	616	cpsYStragal_1_1
10	617	cpsYStragal_2_1
	618	cylBStraga_1_1
	619	cylEStraga_1_1
	620	cylFStraga_1_1
15	621	cylHStraga_1_1
	622	cyllStraga_1_1
	623	cylJStraga_1_1
20	624	cylKStraga_1_1
	625	0487Straga_1_1
	626	0488Straga_1_1
	627	0493Straga_1_1
25	628	0495Straga_1_1
	629	0498Straga_1_1
	630	0500Straga_1_1
30	631	0502Straga_1_1
	632	0504Straga_1_1
	633	foIDStraga_1_1
25	634	neuA1Strgal_1_1
35	635	neuB1Strgal_1_1
	636	neuC1Strgal_1_1
	637	neuD1Strgal_1_1
40	638	recNStraga_1_1
	639	ileSStraga_1_1
	Streptococcus pyogenes identification	
45	645	cyclStrpyog_1_1
	646	fah_rph_hlo_Strpyog_1_1
	647	int_1_1
	648	int315.5_1_1
50	649	murEStrpyog_1_1
	650	oppA_1_1
	651	oppCStrpyog_1_1
55	652	oppD_1_1
	653	SPy0382Strpyog_1_1
	654	SPy0390Strpyog_1_1

		(	
	Streptococcus pyogenes identification		
5	655	SpyM3_1351_1_1	
	656	vicXStrpyog_1_1	
	Streptococcus vi	Streptococcus viridans identification	
	687	573Stprmut_1_1	
10	688	580SStprmut_1_1	
	689	581_582SStprmut_1_1	
	690	584SStprmut_1_1	
_	691	dltAStrmut_1_1	
15	692	dltBStrmut_1_1	
	693	dltCppx1Strmut_1_1	
	694	dltDStrmut_1_1	
20	695	lichStrbov_1_1	
	696	lytRStprmut_1_1	
	697	lytSStprmut_1_1	
05	698	pepQStrrmut_1_1	
25	699	pflCStrmut_1_1	
	700	recNStprmut_1_1	
	701	ytqBStrmut_1_1	
30	Proteus mirabilis	identification	
	706	atfA_1_1	
	707	atfB_1_1	
25	708	atfC_1_1	
35	709	ccmPrmi1_1_1	
	710	cyaPrmi_1_1	
	711	aad_1_1	
40	712	flfB_1_1	
	713	flfD_1_1	
	714	flfN_1_1	
45	715	flhD_1_1	
	716	floA_1_1	
	717	ftsK_1_1	
	718	gstB_1_1	
50	719	hemCPrmi_1_1	
	720	hemDPrmi_1_1	
	721	hev_1_1	
55	722	katA_1_1	
-	723	lpp1_1_1	
	724	menE_1_1	

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		(00111111111111111111111111111111111111
	Proteus mirabilis identification	
	725	mfd_1_1
5	726	nrpA_1_1
	727	nrpB_1_1
	728	nrpG_1_1
10	729	nrpS_1_1
	730	nrpT_1_1
	731	nrpU_1_1
-	732	pat_1_1
15	733	pmfA_1_1
	734	pmfC_1_1
	735	pmfE_1_1
20	736	ppaA_1_1
	737	rsbA_1_1
	738	rsbC_1_1
25	739	speB_1_1
25	740	stmA_1_1
	741	stmB_1_1
	742	terA_1_1
30	743	terD_1_1
	744	umoA_1_1
	745	umoB_1 _1
35	746	umoC_1_1
	747	ureR_1_1
	748	xerC_1_1
	749	ygbA_1_1
40	Proteus vulgaris	identification
	776	envZPrvu_1_1
	777	frdC_1_1
45	778	frdD_1_1
	779	infBPrvu_1_1
	780	lad_1_1
	781	tna2_1_1
50		

## b) virulence gene probes

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SEQ ID NO	Probe
Staphylococcus aureus virulence	
100	bsaE_1_1
101	bsaG_1_1

	\-	
	SEQ ID NO	Probe
5	Staphylococcus	aureus virulence
	102	cap5h_1_1
	103	cap5i_1_1
	104	cap5j_1_1
10	105	cap5k_1_1
	106	cap8H_1_1
	107	cap81_1_1
15	108	cap8J_1_1
	109	cap8K_1_1
	110	l-hld_1_1
	111	I-hysA_1_1
20	112	l-lgGbg_1_1
	113	EDIN_1_1
	114	eta_1_1
25	115	etb_1_1
	116	hgIA_1_1
	117	hgIA_2_1
	118	hglB_1_1
30	119	hglC_2_1
	120	hla_1_1
	121	hlb_1_2
35	122	lukF_1_1
	123	lukS_1_1
	124	lukS_2_1
	125	NAG_1_1
40	126	sak_1_1
	127	sea_1_1
	128	seb_1_1
45	129	sec1_1_1
	130	seg_1_1
	131	seh_1_1
	132	sel_1_1
50	133	set15_1_1
	134	set6_1_1
	135	set7_1_1
55	136	set8_1_1
	137	sprV8_1_1
	138	tst_1_1
•		

	SEQ ID NO	Probe
5	Staphylococcus	aureus virulence
	139	I-sdrC_1_1
	140	I-sdrD_1_1
	141	l-sdrE_1_1
10	Escherichia coli	virulence
	153	b1202_1_1
	154	eae_1_1
15	155	eltB_1_1
	156	escR_1_1
	157	escT_1_1
	158	escU_1_1
20	159	espB_1_1
	160	fes_1_1
	161	fes_2_1
25	162	fteA_1_1
	163	hlyA_1_1
	164	hlyB_1_1
	165	iucA_1_1
30	166	iucB_1_1
	167	iucC_1_1
	168	papG_1_1
35	169	rfbE_1_1
	170	shuA_1_1
	171	SLTII_1_1
	172	toxA-LTPA_1_1
40	173	VT2vaB_1_1
	Staphylococcus epidermidis virulence	
	200	gcaD_1_1
45	201	hld_orf5_1_1
	202	icaC_1_1
	203	icaD_1_1
	204	icaR_1_1
50	205	psm_beta1and2_1_1
	206	purR_1_1
	207	spoVG_1_1
55	208	yabJ_1_1
	Staphylococcus	haemolyticus virulence
	215	lipShaem olyt_1_1

	( -	
	Staphylococcus	<i>lugdunensis</i> virulence
	220	slushABCStalugd_1_1
5	221	fblStalugd_1_1
	Staphylococcus	warneri virulence
	230	gehAStwar_1_1
10	Candida albican	s virulence
	292	CCN1_1_1
	293	CDC28_1_1
_	294	CLN2_1_1
15	295	CPH1_1_1
	296	CYB1_1_1
	297	EFG1_1_1
20	298	MNT1_1_1
	299	RBF1_1_1
	300	RBF1_2_1
05	301	RIM101_1_1
25	302	RIM8_1_1
	303	SEC14_1_1
	304	SEC4_1_1
30	305	TUP1_1_1
	306	YPT1_1_1
	307	ZNF1CZF1_2_1
35	Enterococcus fa	ecalis virulence
	343	asa1_1_1
	344	asp1_1_1
	345	cgh_1_1
40	346	cylA_1_1
	347	cylB_1_1
	348	cyll_1_1
45	349	cylL_cylS_1_1
	350	cylM_1_1
	351	ace_1_1
	352	ef00108_1_1
50	353	ef00109_1_1
	354	ef0011_1_1
	355	ef00113_1_1
55	356	ef0012_1_1
	357	ef0022_1_1
	358	ef0031_1_1

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	Enterococcus fa	ecalis virulence
5	359	ef0032_1_1
	360	ef0040_1_1
	361	ef0058_1_1
	362	enIA_1_1
10	363	esa_1_1
	364	esp_1_1
	365	gelE_1_1
15	366	groEL_1_1
	367	groES_1_1
	368	rt1_1_1
	369	sala_1_1
20	370	salb_1_1
	371	sea1_1_1
	372	sep1_1_1
25	373	vicK_1_1
	374	yycH_1_1
	375	yycl_1_1
	376	yycJ_1_1
30	Enterococcus fa	ecium virulence
	394	entA_entl_1 _1
	395	entD_1_1
35	396	entR_1_1
	397	oep_1_1
	398	sagA_1_2
	Klebsiella pneur	<i>moniae</i> virulence
40	432	cim_1_1
	433	aldA_1 _1
	434	aldA_2_1
45	435	hemly_1_1
	436	pSL017_1_1
	437	pSL020_1_1
	438	rcsA_1_1
50	439	rmIC_1_1
	440	rmID_1_1
	441	waaG_1_1
55	442	wbbD_1_1
	443	wbbM_1_1
	444	wbbN_1_1

	, -	
	Klebsiella pneur	<i>moniae</i> virulence
5	445	wbdA_1_1
Ŭ	446	wbdC_1_1
	447	wztKpn_1_1
	448	yibD_1_1
10	Pseudomonas a	<i>eruginosa</i> virulence
	491	aprA_1_1
	492	aprE_1_1
15	493	ctx_1_2
	494	algB_1_1
	495	algN_1_1
	496	algR_1_1
20	497	ExoS_1_1
	498	fpvA_1_1
	499	lasRa_1_1
25	500	lipA_1_1
	501	lipH_1_1
	502	Orf159_1_2
	503	Orf252_1_1
30	504	pchG_1 _1
	505	PhzA_1_1
	506	PhzB_1_1
35	507	PLC_1_1
	508	plcN_1_1
	509	plcR_1 _1
	510	pvdD_1_1
40	511	pvdF_1_2
	512	pyocinS1_1_1
	513	pyocinS1im_1_1
45	514	pyocinS2_1 _1
	515	pys2_1_1
	516	pys2_2_1
50	517	rbf303_1 _1
50	518	rhlA_1_1
	519	rhlB_1_1
	520	rhIR_1_1
55	521	TnAP41_1_2
	522	toxA_1_1

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	Streptococcus p	neumoniae virulence
	592	igaStrpneu_1_1
5	593	lytA_1_1
	594	nanA_1_1
	595	nanBStrpneu_1_1
10	596	pcpCStrpneu_1_1
	597	ply_1_1
	598	prtAStrpneu_1_1
	599	pspA_1_2
15	600	SP0834Strpneu_1_1
	601	SP0834Strpneu_1_2
	602	sphtraStrpneu_1_1
20	603	wciJStrpneu_1_1
	604	wziyStrpneu_1_1
	605	wzxStrpneu_1_1
	Streptococcus a	galactiae virulence
25	640	CAMPfactor_1_1
	641	CAMPfactor_2_1
	642	0499Straqa_1_1
30	643	hylStragal_1_1
	644	lipStragal_1_1
	Streptococcus pyogenes virulence	
05	657	DNaselStrpyog_1_1
35	658	fba2Strpyog_1_1
	659	fhuAStrpyog_1_1
	660	fhuB1Strpyog_1_1
40	661	fhuDStrpyog_1_1
	662	fhuGStrpyog_1_1
	663	hylA_1_1
45	664	hylP_1_1
***	665	hylp2_1_1
	666	oppB_1_1
	667	ropB_1_1
50	668	scpAStrpyog_1_1
	669	sloStrpyog_1_1
	670	smez-4Strpyog_1_1
55	671	sof_1_1
55	672	sof_2_1
	673	speA_1_1

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	Streptococcus p	yogenes virulence
	674	speB2Strpyog_1_1
5	675	speCStrpyog_1_1
	676	speJStrpyog_1_1
	677	srtBStrpyog_1_1
10	678	srtCStrpyog_1_1
	679	srtEStrpyog_1_1
	680	srtFStrpyog_1_1
_	681	srtGStrpyog_1_1
15	682	srtlStrpyog_1_1
	683	srtKStrpyog_1_1
	684	srtRStrpyog_1_1
20	685	srtTStrpyog_1_1
	686	vicKStrpyog_1_1
	Streptococcus v	<i>iridans</i> virulence
25	702	hlyXStrmut_1_1
25	703	igaStrmitis_1_1
	704	igaStrsanguis_1_1
	705	perMStrmut_1_1
30	Proteus mirabilis	s virulence
	750	flaA_1_1
	751	flaD_1_1
35	752	fliA_1_1
	753	hpmA_1_1
	754	hpmB_1_1
	755	lpsPrmi_1_1
40	756	mrpA_1_1
	757	mrpB_1_1
	758	mrpC_1_1
45	759	mrpD_1_1
	760	mrpE_1_1
	761	mrpF_1_1
	762	mrpG_1_1
50	763	mrpH_1_1
	764	mrpl_1_1
	765	mrpJ_1_1
55	766	patA_1_1
	767	putA_1_1
	768	uca_1_1

(continued)

Proteus mirabilis virulence	
769	ureDPrmi_1_1
770	ureEPrmi_1_1
771	ureFPrmi_1_1
772	zapA_1_1
773	zapB_1_1
774	zapD_1_1
775	zapE_1_1
Proteus vulgaris virulence	
782	end_1_1
783	pqrA_1_1
784	urg_1_1

c) resistance gene probes

SEQ ID NO	Probe		
Beta-lactams resistance			
785	blaIMP-7_1_1		
786	meclSepid_1_1		
787	blaOXA-10_1_2		
788	blaB_1_1		
789	ampC_1_1		
790	I-blaR_1_1		
791	blaOXA-32_1_1		
792	bla-CTX-M-22_1_1		
793	pbp2aStrpneu_1_1		
794	blaSHV-1_1_1		
795	blaOXA-2_1_1		
796	blaRShaemolyt_1_1		
797	blalMP-7_1_2		
798	I-mecR_1_1		
799	blaOXY_1_1		
800	dacCStrpyog_1_1		
801	femA_1_1		
802	mecA_1_1		
803	blalShaemolyt_1_1		
804	blavim_1_1		
805	pbp2b_1_1		
806	pbp2primeSepid_1_1		
807	pbp2x_1_1		

5	SEQ ID NO	Probe
	Beta-lactams resistance	
	808	pbp3Saureuc_1_1
	809	pbp4_1_1
10	810	pbp5Efaecium_1_1
	811	pbpC_1_1
	812	I-mecl_1_1
15	813	pbp1a_1_1
	814	I-blal_1_1
	815	blaTEM-106_1_1
	816	blaOXY-KLOX_1_1
20	817	ftsWEF_1_1
	818	fmhB_1_1
	819	cumA_1_1
25	820	fem BShaem olyt_1_1
	821	blaPER-1_1_1
	822	bla_FOX-3_1_1
	823	blaA_1_1
	824	psrb_1_1
30	825	fmhA_1_1
	826	mecRiSepid_1_1
35	827	blaZ_1_1
	828	blaOXA-1_1_1
	829	fox-6_1_1
	830	blaPrmi_1_1
	Aminoglycosides resistance	
40	831	aacA_aphDStwar_1_1
	832	aacC1_1_2
45	833	aacC2_1_1
	834	strB_1_1
	835	aadA_1_1
	836	aadB_1_2
50	837	aadD_1_1
	838	aacA4_1_2
	839	strA_1_1
55	840	aph-A3_1_1
	841	aacC1_1_1
	842	aacA4_1_1
	843	aacA-aphD_1_1

(continued)

Aminoglycosides resistance		
844	I-spc_1_1	
845	aphA3_1_1	
Macrolide-Lincosamide-Streptogramin resistance		
846	ermC_1_1	
847	linB_1_1	
848	satSA_1_1	
849	mdrSA_1_1	
850	I-linA_1_1	
851	ermB_1_2	
852	ermA_1_1	
853	satA_1_1	
854	msrA_1_1	
855	mphBM_1_1	
856	mefA_1_1	
857	mrx_1_1	
Trymethoprim resistance		
858	dfrStrpneu_1_1	
859	dfrA_1_1	
Chloramphenicol resistance		
860	cmlA5_1_1	
861	catEfaecium_1_1	
862	cat_1_1	
Tetracyclines resistance		
863	tetAJ_1_1	
864	tetL_1_1	
865	tetM_1_1	
Glycopeptides resistance		
866	vanH(tn)_1_1	
867	vanA_1_1	
868	vanHB2_1_1	
869	vanR_1_1	
870	vanRB2_1_1	
871	vanS(tn)_1_1	
872	vanSB2_1_1	
873	vanWB2_1_1	
874	ddl_1_1	
875	ble_1_1	
876	vanXB2_1_1	

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	·	·
	Glycopeptides resista	ince
5	877	vanY(tn)_1_1
	878	vanYB2_1_1
	879	vanB_1_1
	880	vanZ(tn)_1_1
10	881	vanC-2_1_1
	882	vanX(tn)_1_1
	Other / multiple subst	ances resistance
15	883	acrB_1_1
	884	mexB_1_2
	885	I-qacA_1_1
	886	sull_1_1
20	887	sul_1_1
	888	cadBStalugd_1_1
	889	mexA_1_1
25	890	acrR_1_1
	891	emeA_1_1
	892	acrA_1_1
	893	rtn_1_1
30	894	abcXStrpmut_1_1
	895	qacEdelta1_1_1
	896	elkT-abcA_1_1
35	897	I-cadA_1_1
	898	albA_1_1
	899	wzm_1_1
	900	msrCb_1_1
40	901	nov_1_1
	902	wzt_1_1
	903	wbbl_1_1
45	904	norA23_1_1
	905	mexR_1_1
	906	arr2_1_1
50	907	mreA_1_1
50	908	I-cadC_1_1
	909	uvrA_1_1
	Candida albicans dru	g resistance
55	910	CRD2_1_1
	911	CDR1_1_1

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Candida albicans drug resistance							
912	CDR1_2_1						
913	MET3_1_1						
914	FET3_1_1						
915	FTR2_1 _1						
916	MDR1-7_1_1						
917	ERG11_1_1						
918	SEC20_1_1						

15	d) controls and utility genes
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SEQIDNO	Probe
Negative Cor	
919	rbcL_1_1
925	rbcL_1_1 1_2
Positive cont	rols / human genes
920	LDHA(hu)_1_1
921	GAPD(hu)_1_1
922	b-Act(hu)_1_1
923	ARHGDIA(hu)_1_1
924	PGK1 (hu)_1_1
Positive cont	rols / 16S
926	16SPa_1_1
927	23SEfaecium_2_1
928	16SStrepyog_1_1
929	16SStrepneu_1_1
930	16SStrepagalactiae_1_1
931	16SEfaecium_1_1
932	16SEfaecium_2_1
933	16SRNAEf_2_1
934	16SKpn_1_1
935	16SSa_3_1
936	16SRNAEf_1 _1
937	16SShominis_1_1
938	16SShaemolyt_1_1
939	23SEfaecium_1_1
940	16SrRNAPrmi_1_1
941	16SrRNAPrvu1_1_1

(continued)

Positive cont	Positive controls / 16S								
942	16SSa_1_1								
943	16SKlox_1_1								
Positive cont	rols / Spiked Controls								
944	p53_1_1								
945	0135mihck_1_1								
946	FAN_1_1								
947	0270cap_1_1								

[0059] The DNA microarray of (1) is preferably suitable for

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(I) identification of *Staphylococcus aureus* and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:1-99, preferably at least the gene probes represented by SEQ ID NO:71 and 68; and/or (II) identification of *Escherichia coli* and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:142-152, preferably at least the gene probes represented by SEQ ID NO: 143 and 149; and/or

(III) identification of *Staphylococcus epidermidis* and comprises gene probes of group (a) selected from SEQ ID NO:174-199, preferably at least the gene probes represented by SEQ I D NO: 177 and 184; and/or

(IV) identification of *Staphylococcus haemolyticus* and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:209-214, preferably at least the gene probes represented by SEQ I D NO:209 and 210; and/or

(V) identification of Staphylococcus lugdunensis and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:216-219, preferably at least the gene probes represented by SEQ ID NO:216 and 219; and/or (VI) identification of Staphylococcus warneri and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:224-229, preferably at least the gene probes represented by SEQ ID NO:224 and 225; and/or (VII) identification of Candida albicans and comprises one or more or all gene probes of group (a) selected from SEQ I D NO:231-291, preferably at least the gene probes represented by SEQ I D NO:231 and 232; and/or (VIII) identification of Enterococcus faecalis and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:308-342, preferably at least the gene probes represented by SEQ ID NO:308 and 310; and/or (IX) identification of Enterococcus faecium and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:377-393, preferably at least the gene probes represented by SEQ ID NO:377 and 380; and/or (X) identification of Klebsiella pneumonia and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:399-431, preferably at least the gene probes represented by SEQ ID NO:399 and 402; and/or (XI) identification of Klebsiella oxytoca and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:449-469, preferably at least the gene probes represented by SEQ I D NO:449 and 455; and/or (XII) identification of Pseudomonas aeruginosa and comprises one or more or all gene probes of group (a) selected from SEQ I D NO:470-490, preferably at least the gene probes represented by SEQ I D NO:470 and 471; and/or (XIII) identification of Streptococcus pneumoniae and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:523-591, preferably at least the gene probes represented by SEQ ID NO:523 and 524; and/or (XIV) identification of Streptococcus agalactiae and comprises one or more or all gene probes of group (a) selected from SEQ I D NO:606-639, preferably at least the gene probes represented by SEQ I D NO:606 and 619; and/or (XV) identification of Streptococcus pyogenes and comprises one or more or all gene probes of group (a) selected from SEQ I D NO:645-656, preferably at least the gene probes represented by SEQ I D NO:645 and 646; and/or (XVI) identification of Streptococcus viridans and comprises one or more or all gene probes of group (a) selected from SEQ ID NO:687-701, preferably at least the gene probes represented by SEQ I D NO:687 and 691; and/or (XVII) identification of *Proteus mirabilis* and comprises one or more or all gene probes of group (a) selected from SEQ I D NO:706-749, preferably at least the gene probes represented by SEQ I D NO:706 and 710; and/or (XVIII) identification of Proteus vulgaris and comprises one or more or all gene probes of group (a) selected from SEQ I D NO:776-781, preferably at least the gene probes represented by SEQ I D NO:776 and 777.

[0060] In a further especially preferred aspect, the DNA m icroarray of (1) is suitable for

(I) virulence determination of Staphylococcus aureus and comprises one or more or all of the gene probes of group

- (b) selected from SEQ ID NO:100-141; and/or
- (II) virulence determination of *Escherichia coli* and comprises one or more or all of the gene probes of group (b) selected from SEQ I D NO: 153-173; and/or
- (III) virulence determination of *Staphylococcus epidermidis* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:200-208; and/or
- (IV) virulence determination of *Staphylococcus haemolyticus* and comprises the gene probe of group (b) represented by SEQ I D NO:215; and/or
- (V) virulence determination of *Staphylococcus lugdunensis* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:220-221; and/or
- (VI) virulence determination of *Staphylococcus warneri* and comprises the gene probe of group (b) represented by SEQ I D NO:230; and/or
- (VII) virulence determination of *Candida albicans* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:292-307; and/or
- (VIII) virulence determination of *Enterococcus faecalis* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:343-376; and/or
- (IX) virulence determination of *Enterococcus faecium* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:394-398; and/or
- (X) virulence determination of *Klebsiella pneumonia* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:432-448; and/or
- (XI) virulence determination of Klebsiella oxytoca; and/or
- (XII) virulence determination of *Pseudomonas aeruginosa* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:491-522; and/or
- (XIII) virulence determination of *Streptococcus pneumoniae* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:592-605; and/or
- (XIV) virulence determination of *Streptococcus agalactiae* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:640-644; and/or
- (XV) virulence determination of *Streptococcus pyogenes* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:657-686; and/or
- (XVI) virulence determination of *Streptococcus viridans* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:702-705; and/or
- (XVII) virulence determination of *Proteus mirabilis* and comprises one or more or all of the gene probes of group (b) selected from SEQ ID NO:750-775; and/or
- (XVIII) virulence determination of *Proteus vulgaris* and comprises one or more or all of the gene probes of group (b) selected from SEQ I D NO: 782-784.

[0061] In a further especially preferred aspect, the DNA m icroarray of (1) is suitable for antibiotic resistance determination of (I) Staphylococcus aureus, (II) Escherichia coli, (III) Staphylococcus epidermidis, (IV) Staphylococcus haemolyticus, (V) Staphylococcus lugdunensis, (VI) Staphylococcus warneri, (VIII) Enterococcus faecalis, (IX) Enterococcus faecium, (X) Klebsiella pneumonia, (XI) Klebsiella oxytoca, (XII) Pseudomonas aeruginosa, (XIII) Streptococcus pneumoniae, (XIV) Streptococcus agalactiae, (XV) Streptococcus pyogenes, (XVI) Streptococcus viridans, (XVII) Proteus mirabilis, and/or (XVIII) Proteus vulgaris and comprises one or more or all of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or

[0062] it is suitable for antibiotic resistance determination of (VII) *Candida albicans* and comprises one or more or all of the gene probes of group (c) selected from SEQ ID NO:910-918.

[0063] In a preferred embodiment, the microarray of (1) is suitable for identification and characterisation, i.e. virulence and/or resistance determination, of the target microorganism and comprises one or more or all of the gene probes of group (a) and additionally one or more or all of the gene probes of group (b) and group (c) for each organism as listed above [0064] If the identification and/or characterisation of *S. aureus, E. coli* and/or *P. aeruginosa* is the aim of a test using the array, then the array comprises preferably at least the core gene probes designated in example 7, more preferably all the sequences listed in Tab. 2 and/or Tab. 6. Even more preferred, it consists of said sequences.

**[0065]** In a most especially preferred aspect, the DNA microarray of (1) comprises the following gene probes, even more preferably consists of the following gene probes:

- (I) When the DNA microarray is suitable for identification and characterisation of Staphylococcus aureus, it comprises
  - (a) the gene probes represented by SEQ I D NO: 1-99; and
  - (b) the gene probes represented by SEQ I D NO:100-141 and/or
  - (c) the gene probes represented by SEQ I D NO:785-909.

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	(II) When the DNA microarray is suitable for identification and characterisation of Escherichia coli, it comprises
	(a) the gene probes represented by SEQ ID NO: 142-152; and
	(b) the gene probes represented by SEQ I D NO: 153-173 and/or
5	(c) the gene probes represented by SEQ I D NO: 785-909.
	(III) When the DNA microarray is suitable for identification and characterisation of <i>Staphylococcus epidermidis</i> , it comprises
10	<ul><li>(a) the gene probes represented by SEQ I D NO: 174-199; and</li><li>(b) the gene probes represented by SEQ I D NO: 200-208 and/or</li><li>(c) the gene probes represented by SEQ I D NO: 785-909.</li></ul>
15	(IV) When the DNA m icroarray is suitable for identification and characterisation of <i>Staphylococcus haemolyticus</i> , it comprises
20	<ul><li>(a) the gene probes represented by SEQ I D NO: 209-214; and</li><li>(b) the gene probes represented by SEQ I D NO: 215 and/or</li><li>(c) the gene probes represented by SEQ I D NO: 785-909.</li></ul>
	(V) When the DNA microarray is suitable for identification and characterisation of <i>Staphylococcus lugdunensis</i> , it comprises
	(a) the gene probes represented by SEQ I D NO: 216-219; and
25	(b) the gene probes represented by SEQ I D NO: 220-221 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
30	(VI) When the DNA m icroarray is suitable for identification and characterisation of <i>Staphylococcus warneri</i> , it comprises
00	(a) the gene probes represented by SEQ I D NO: 224-229; and
	(b) the gene probes represented by SEQ I D NO: 230 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
35	(VII) When the DNA microarray is suitable for identification and characterisation of Candida albicans, it comprises
	(a) the gene probes represented by SEQ I D NO: 231 -291; and
	(b) the gene probes represented by SEQ ID NO: 292-307 and/or
	(c) the gene probes represented by SEQ ID NO: 910-918.
40	(VIII) When the DNA microarray is suitable for identification and characterisation of <i>Enterococcus faecalis</i> , it comprises
	(a) the gene probes represented by SEQ I D NO: 308-342; and
45	(b) the gene probes represented by SEQ ID NO: 343-376 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
	(IX) When the DNA microarray is suitable for identification and characterisation of <i>Enterococcus faecium</i> , it comprises
50	(a) the gene probes represented by SEQ I D NO: 377-393; and
	(b) the gene probes represented by SEQ I D NO: 394-398 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
<i>55</i>	(X) When the DNA microarray is suitable for identification and characterisation of <i>Klebsiella pneumonia</i> , it comprises
	(a) the gene probes represented by SEQ I D NO: 399-431; and
	(b) the gene probes represented by SEQ ID NO: 432-448 and/or
	(c) the gane probes represented by SEO LD NO: 785-909

	(XI) When the DNA microarray is suitable for identification and characterisation of Klebsiella oxytoca, it comprises
_	(a) the gene probes represented by SEQ I D NO: 449-469, and (c) the gene probes represented by SEQ I D NO: 785-909.
5	(XII) When the DNA microarray is suitable for identification and characterisation of <i>Pseudomonas aeruginosa</i> , it comprises
10	(a) the gene probes represented by SEQ I D NO: 470-490; and (b) the gene probes represented by SEQ I D NO: 491 -522 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
15	(XIII) When the DNA microarray is suitable for identification and characterisation of <i>Streptococcus pneumoniae</i> , it comprises
	(a) the gene probes represented by SEQ I D NO: 523-591; and
	(b) the gene probes represented by SEQ I D NO: 592-605 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
20	(XIV) When the DNA microarray is suitable for identification and characterisation of <i>Streptococcus agalactiae</i> , it comprises
	(a) the gene probes represented by SEQ I D NO: 606-639; and
25	<ul><li>(b) the gene probes represented by SEQ I D NO: 640-644 and/or</li><li>(c) the gene probes represented by SEQ I D NO: 785-909.</li></ul>
	(c) the gene probes represented by GEQ 1 D NO. 105-303.
	(XV) When the DNA microarray is suitable for identification and characterisation of <i>Streptococcus pyogenes</i> , it comprises
30	(a) the gene probes represented by SEQ I D NO: 645-656; and
	(b) the gene probes represented by SEQ ID NO: 657-686 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
	(XVI) When the DNA microarray is suitable for identification and characterisation of Streptococcus viridans, it
35	comprises
	(a) the gene probes represented by SEQ I D NO: 687-701; and
	(b) the gene probes represented by SEQ I D NO: 702-705 and/or (c) the gene probes represented by SEQ I D NO: 785-909.
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	(XVII) When the DNA microarray is suitable for identification and characterisation of <i>Proteus mirabilis</i> , it comprises
	(a) the gene probes represented by SEQ I D NO: 706-749; and
45	(b) the gene probes represented by SEQ I D NO: 750-775 and/or
45	(c) the gene probes represented by SEQ I D NO: 785-909.
	(XVIII) When the DNA microarray is suitable for identification and characterisation of <i>Proteus vulgaris</i> , it comprises
	(a) the gene probes represented by SEQ I D NO: 776-781; and
50	(b) the gene probes represented by SEQ I D NO: 782-784 and/or
	(c) the gene probes represented by SEQ I D NO: 785-909.
55	[0066] The microarray of embodiment (1) can be fabricated using textbook methods for microarray production, including printing with fine-pointed pins onto the solid support, photolithography using pre-made masks or dynamic micromirror devices, ink-jet printing or electrochemistry on microelectrode arrays (Müller, HJ., Röder, T., "Der Experimentator: Microarrays, Spektrum Akademischer Verlag, Heidelberg (2004)). Preferred fabrication methods are printing methods spotting the gene probes onto the solid surface of the microarray. The attachment of the spotted DNA to the surface is
	achieved by covalent or non-covalent binding, preferably by non-covalent binding, more preferably by electrostatic

interaction (ionic binding), most preferably by ionic binding of the DNA to amino groups present on the surface of the solid support. Any amino-functionalized microarray support can be used, but gamma aminopropyl silane (GAPS™) coated slides, especially UltraGAPS™ coated glass slides, are preferred in present invention.

[0067] The amount of DNA per spot printed onto the array is from 0.1 to 15.0 ng, preferably from 0.1 to 0.2 ng.

[0068] Thus, the present invention also pertains to a method for fabrication of a microarray of embodiment (1), which method comprises spotting the gene probes listed above to an appropriate solid support.

**[0069]** The sample or clinical specimen of embodiment (1) is preferably selected from the group consisting of whole blood, serum, urine, saliva, liquor, sputum, punktate, stool, pus, wound fluid and positive blood cultures, more preferably is whole blood or a positive blood culture, most preferably is a positive blood culture. If blood culture is used as DNA source, 0.5 ml positive blood culture is sufficient for identification and characterisation of the microorganisms and bacteria present without prior amplification of the target DNA.

[0070] Thus, the microarray of present application is

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- (i) a robust diagnostic tool, detecting all tested bacterial reference strains and clinical isolates;
- (ii) sensitive enough to yield positive signals with e.g. only 20 ng of purified genomic *S. aureus* DNA or 2 μg of DNA extracted from blood culture which contains a high percentage of human DNA;
- (iii) highly specific, distinguishing e.g. *S. aureus* from distantly related gram-negative bacteria like *Escherichia coli* or *Pseudomonas aeruginosa* as well as from closely related CoNS;
- (iv) precise enough to identify virulence factors and antibiotic resistance determinant genes without previous amplification by PCR.

**[0071]** Moreover, the whole procedure can be accomplished the same day after blood cultures become positive (e.g. in the Bactec®). Rapid identification of the causative pathogen in fungemia, bacteremia and sepsis is crucial for several reasons:

- (i) appropriate antimicrobial therapy should be started as early as possible and unnecessary treatment avoided;
- (ii) the prognosis of the patients with sepsis may be improved; and
- (iii) expenditures on antimicrobials and prolonged hospitalisation can be reduced.

[0072] With the gene-segment based microarray of (1) there is an excellent correlation between genotypic detection of antibiotic resistance determinants and phenotypic typing using conventional susceptibility testing. In one aspect of the invention, the detection of the resistance genes *mecA*, *blaZ*, *ermA*, *ermC*, *msrSA*, *aadD* and *aacA-aphD* by microarray hybridisation allows for reliable prediction of oxacillin, penicillin, erythromycin, tobramycin and gentamicin resistance in a single assay

**[0073]** By microarray hybridisation according to present invention it is furthermore possible to discriminate multi-resistant and multi-susceptible MRSA (strain MW2). Multi-susceptible MRSA have been shown to be susceptible to tobramycin and erythromycin (Polyzou, A. et al., J. Antimicrob. Chemother. 48:231-4 (2001); Pournaras, S. et al., J. Clin. Microbiol. 39:779-81 (2001)).

**[0074]** In a preferred aspect of the invention, simultaneous comprehensive resistance genotyping for oxacillin, macrolide and aminoglycoside resistance genes (preferably *mecA*, *aadD*, *aacA-aphD*, *ermA*, *B*, *C* and *msrSA*) by microarray hybridisation allows the rapid discrimination of multi-resistant or multi-susceptible strains and in consequence other therapeutic options with e.g. macrolides and may reduce reliance on vancomycin (Polyzou, A. et al., J. Antimicrob. Chemother. 48:231-4 (2001); Pournaras, S. et al., J. Clin. Microbiol. 39:779-81 (2001)).

[0075] One preferred aspect of embodiment (1) is a DNA microarray for the identification and characterisation of the three important bacteremia causing species *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* in a sample, preferably in blood culture. The microarray allows simultaneous species identification and detection of important virulence and antibiotic resistance genes in a single assay. Preferably, this array consists of 2-20 species specific gene probes, 1-20 virulence gene probes and 1-20 resistance gene probes of at least 100 nt length, more preferably of 200-800 nt length. One especially preferred embodiment is an array comprising or consisting of the gene probes listed in Tab. 2. The probes may be amplified from recombinant plasmids or synthesized by any other method know in the art. These probes represent genes encoding house-keeping proteins, virulence factors and antibiotic resistance determinants. Evaluation with 42 clinical isolates, 3 reference strains and 13 positive blood cultures revealed that this DNA microarray is highly specific in identifying *S. aureus*, *E. coli* and *P. aeruginosa* strains and in discriminating them from closely related Gram-positive and Gram-negative bacterial strains also known to be etiological agents of bacteremia. In Example 6 and 7, this array was successful in identifying all tested 27 *E. coli*, *P. aeruginosa* and *S. aureus* strains and in discriminating them from 21 closely related Gram positive and Gram negative bacterial strains. There is a nearly perfect correlation between genotypic antibiotic resistance by hybridisation to the *S. aureus* resistance gene probes *mecA* (oxacillin/methicillin resistance), *aacA-aphD* (gentamicin resistance), *ermA* (erythromycin resistance)

and *blaZ* (penicillin resistance) and the *E. coli* resistance gene probes *blaTEM-106* (penicillin resistance) and *aacC2* (aminoglycoside resistance) and phenotypic antibiotic resistance determined by conventional susceptibility testing (Example 10).

[0076] One further preferred aspect of embodiment (1) of the invention is a DNA microrarray for the identification and characterisation of *S. aureus* in a sample, preferably in blood culture. Evaluation with 10 clinical isolates, 6 reference strains and 10 positive blood cultures revealed that this DNA microarray is highly specific in identifying *S. aureus* and in discriminating them from closely related Gram-positive and Gram-negative bacterial strains also known to be etiological agents of bacterem ia (Example 11).

[0077] The method of embodiment (3) comprises - after isolating the total DNA (including non-microbial DNA) from a sample - the steps of immediate labelling and microarray-based detection of this isolated DNA with or without, preferably without, further DNA amplification steps after the DNA isolation. It is one advantage of the method (3) that it can be performed without said further DNA amplification steps, i.e. the isolated DNA is labelled and applied to the microarray without prior amplification. The use of a single protocol for all microbial species comprising all steps of a microarray procedure including DNA preparation and DNA-chip hybridisation, is essential for testing blood cultures or other clinical specimens, where the bacterial diagnosis is usually uncertain. Preferably, a DNA preparation protocol employing sonication for simultaneous cell disruption and target DNA fragmentation is the method of choice to increase the sensitivity of the microarray, in particular towards low-copy number and/or plasmid encoded genes which may be underrepresented in the target DNA.

**[0078]** The method of embodiment (3) is preferably a method for diagnosis of bacteremia or sepsis. Furthermore, the sample or clinical specimen used in embodiment (3) is preferably blood or derived from blood, more preferably is a blood culture. Most preferably, the clinical specimen is a positive blood culture.

[0079] To obtain positive signals in the method of embodiment (3), 100 pg of purified genomic microbial DNA may be sufficient (lower detection limit), but preferably at least 1 ng of said DNA should be present in the sample. Usually, at least 10 ng, preferably at least 20 ng, more preferably at least 1  $\mu$ g of purified genomic microbial DNA or at least 1  $\mu$ g, preferably at least 2  $\mu$ g of DNA extracted from blood culture are required. 500  $\mu$ l of positive blood culture yield enough DNA for several hybridisations.

[0080] In the method of embodiment (3), the ratio of microbial DNA to total DNA isolated from said sample or clinical specimen is less than or equal to 100 %, preferably is from 1% to 99%, m ore preferably from 30 to 60%.

[0081] The labelling reaction of the method of embodiment (3) may be any DNA labelling reaction known in the art. However, chemical labelling reactions consisting of chemical attachement of a reporter molecule to the sample DNA and labelling by integration of labelled nucleotides into the sample DNA are preferred. Preferably the reporter molecules are fluorophores, more preferably are of the cyanine group of fluorophores. Most preferably, the DNA is labelled with Cy3, Cy5 and/or Alexa Fluor 647 and Alexa Fluor 546. The ratio of bases to dye molecules (BDR) is preferably less or equal to 60.

**[0082]** The detection of the reporter molecule in the method of embodiment (3) of the invention is preferably done by using a suitable detection system for the bound reporter molecule. This detection system is preferably based on visualization of the reporter molecule, more preferably on fluorescence detection. Furthermore, the detection is preferably done by a microarray scanner.

[0083] In the method of embodiment (3) of the invention, the DNA microarray can be substituted by any other solid support onto which DNA gene probes are attached in a way permitting hybridisation of the DNA in the sample and subsequent detection of the bound DNA. This includes the use of microtiter plates coated with one or several DNA gene probes per well, of glass surfaces (like, e.g., microscopic slides) with DNA spots, of filter paper disks, membranes, gold electrodes and beads (particles with a diameter of from 1 nm to several  $\mu$ m made of glass, plastic, metal etc.) coated with DNA, etc.

[0084] The kit of embodiment (4) of the invention may additionally comprise reagents for the labelling reactions of embodiment (3) and/or reagents necessary for the hybridisation step of the method of embodiment (3).

[0085] The present invention is described in more detail by reference to the following examples. It should be understood that these examples are for illustrative purpose only and are not to be construed as limiting the invention.

## 50 Examples

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**[0086]** In the experimental examples described below, standard techniques of recombinant DNA technology were used that were described in various publications, e.g. Sambrook et al. (1989), Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, or Ausubel et al. (1987), Current Protocols in Molecular Biology 1987-1988, Wiley Interscience. Unless otherwise indicated, all enzymes and kits were used according to the manufacturers' specifications.

### Example 1: Materials and Methods

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[0087] Reference strains, clinical isolates and culture conditions: Bacterial reference strains were obtained from the American Type Culture Collection (ATCC, Manassas, Va.), the Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ, Braunschweig, Germany) or the network on antimicrobial resistance in *Staphylococcus aureus* (NARSA, Herndon, Virginia). Clinical isolates were obtained from the inventors' clinical routine microbiology laboratory.

[0088] The following bacteria were used for evaluation of the specificity of the microarray in Examples 2-10: Staphylococcus aureus (ATCC 25923, NRS123 alias MW2, 5 clinical isolates), Staphylococcus epidermidis (5 clinical isolates), Staphylococcus capitis (clinical isolate), Staphylococcus haemolyticus (clinical isolate), Staphylococcus hominis (clinical isolate), Staphylococcus warneri (clinical isolate), Staphylococcus auricularis (clinical isolate), Micrococcus spp. (clinical isolate), Escherichia coli (ATCC 25922, 6 clinical isolates), Pseudomonas aeruginosa (ATCC27853, 5 clinical isolates), Klebsiella pneumoniae (3 clinical isolates), Proteus mirabilis (2 clinical isolates), Serratia marcescens (2 clinical isolates), Enterobacter cloacae (clinical isolate), Enterobacter aerogenes (clinical isolate), Acinetobacter baumannii (clinical isolate), Stenotrophomonas maltophilia (clinical isolate), Enterococcus spp. (clinical isolate), Enterococcus faecalis (clinical isolate) and Streptococcus pneumoniae (clinical isolate).

[0089] Bacterial strains and clinical isolates were grown over night at 37 °C with constant shaking in 5 ml Luria-Bertani (LB) broth or tryptic soy broth (TSB, 30 g/l, Merck) containing 3 g/l yeast extract. Enterococci and streptococci were grown in 10 ml TSB plus yeast without agitation under 5% CO<sub>2</sub>. Overnight cultures were harvested at 2,560 g for 10 min. After discarding the supernatant the pellet was washed in 1 ml TE (10 mM Tris-HCl, pH 7.5 and 1 mM EDTA) and recovered by centrifugation at 17,900 g for 10 min. Cell pellets were used for DNA preparation.

[0090] Blood cultures: Aerobic and anaerobic blood culture bottles (BACTEC®, Becton Dickinson, Heidelberg, Germany) were inoculated with blood from patients with suspected sepsis and placed in a BACTEC® 9240 blood culture system (Becton Dickinson), a continuous-reading, automated, and computed blood culture system that detects the growth of microorganisms by monitoring CO<sub>2</sub> production. Incubation was performed according to the manufacturer's recommendations. Bottles with a positive growth index were removed from the incubator, and aliquots of 1 ml of the blood culture suspensions were taken aseptically with a needle syringe. 1 ml-aliquots of the blood culture suspensions were mixed with 1 ml 0.1% Triton®-X-100 and kept at room temperature for 5 min in order to disrupt human blood cells. Bacterial cells were then harvested at 17,900 g for 10 min, pellets were washed in 1 ml TE, recovered by centrifugation and used for DNA preparation. For conventional identification and susceptibility testing, a second 1 ml-aliquot was examined by Gram-stain and subcultured on agar plates. The organisms grown on agar plates were characterised and tested for susceptibility using a VITEK-2 system (bioMerieux, Inc., Nürtingen, Germany), Etest strips (AB BIODISK, Solna, Sweden) or disk diffusion tests following the method recommended by the National Committee for Clinical Laboratory Standards (NCCLS) (Standards, N.C.f.C.L., Approved standard M2-4a, Villanova, PA (1990)).

[0091] For microarray hybridisation experiments, DNA was prepared from 13 blood cultures positive for *S. aureus* (4), *S. epidermidis* (3), *S. pneumoniae* (2), *P. aeruginosa* (1), *E. coli* (2) and *P. mirabilis* (1).

### Example 2: DNA preparation

[0092] Total cellular DNA was extracted and purified either by using the First-DNA All-tissue kit (GEN-IAL GmbH, Troisdorf, Germany) following the instructions of the supplier or by enzymatic lysis followed by phenol/chloroform extraction. For the latter protocol, cell pellets were resuspended in 500 μl lysis buffer (20 mM Tris-HCI, pH 8.0, 2 mM EDTA, pH 8.0, and 1.2% Triton®-X-100) and lysozyme (Sigma, Taufkirchen, Germany) was added to reach a final concentration of 0.8 mg/ml. In addition, lysostaphin (Sigma) was added to a final concentration of 0.2 mg/ml to promote staphylococcal lysis or mutanolysin (0.5 U/μl; Sigma) was added to lyse Streptococci and Enterococci. After incubation at 37°C for one hour, cell lysates were treated with Proteinase K (1 mg/ml; Sigma) for 1 hour at 55°C and then with RNase A (0.2 mg/ml; Qiagen, Hilden, Germany) for 1 hour at 37°C. The volume was increased by the addition of 200 μl TE and the salt concentration was adjusted to 0.7 M by addition of 5 M NaCl. A 10% CTAB (cetyltrimethylammonium bromide) solution in 0.7 M NaCl was added to a final concentration of 1% and incubated at 65°C for 20 min in order to release DNA from polysaccharide DNA complexes. DNA was then extracted once with phenol/chloroform/isoamyl alcohol (25:24:1) and once with chloroform/isoamyl alcohol (24:1) prior to precipitation with one volume of isopropanol. After centrifugation at 17,900 g for 30 min, DNA pellets were washed in 70% ethanol and resuspended in 50-100 μl TE. [0093] Concentration, purity and size of the purified DNA preparations were determined by UV-spectrophotometry (lambda 40, PerkinElmer, Boston USA) and 1% agarose gel electrophoresis.

### Example 3: DNA labelling

[0094] Total DNA from commercially available reference strains, clinical isolates and blood cultures was labelled by a non-enzymatic chemical labelling method using the Label It Cy3/Cy5 kits (Mirus, Madison, USA) or the ULYSIS Alexa

Fluor 467 Nucleic Acid Labelling Kit (Molecular Probes; Eugene, USA). Prior to labelling, each target DNA was spiked with three gene segments (1 µl each, 30 ng/µl) amplified by PCR from selected recombinant plasmids to serve as internal positive controls.

[0095] For labelling with the Label It Cy3/Cy5 kit 5 μg of high molecular weight DNA (>20 kb) were mixed with 7.5 μl reagent in a total volume of 50 µl and incubated for 2 hours at 37°C according to the recommendations by the supplier. After adjusting the volume to 200 µl with H<sub>2</sub>O and adding 0.1 volume of 5 M NaCl, unbound label was removed by precipitation with 2 volumes of ice-cold absolute ethanol for at least 30 min at -20 °C. The labelled DNA was recovered by centrifugation at 17,900 g for 30 min. The pellet was washed with 70% ethanol and resuspended in 70 µl TE.

[0096] For labelling with the Ulysis Alexa Fluor 647 kit, 1 μg DNA was denatured at 95°C for 5 min, cooled on ice, mixed with 20 µl labelling buffer and 5 µl reagent and incubated at 80 °C for 15 min according to the instructions of the manufacturer. Unbound dye was removed by ethanol precipitation as described above. The relative labelling efficiency of a reaction was evaluated by calculating the approximate ratio of bases to dye molecules (acceptable labelling ratios for nucleic acid were =60). This ratio and the amount of recovered labelled DNA was determined by measuring the absorbance of the nucleic acids at 260 nm and the absorbance of the dye at its absorbance maximum using a lambda40 UV-spectrophotometer (PerkinElmer) and plastic disposable cuvettes for the range from 220 nm to 1,600 nm (UVette; Eppendorf, Hamburg, Germany).

### Example 4: Microarray construction

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20 [0097] Cloned PCR-products were used to generate probes for the DNA microarray. All together 120 gene segments representing virulence genes, antibiotic resistant determinants and species specific metabolic and structural genes from S. aureus (40), E. coli (31) and P. aeruginosa (49) were represented on the microarray (Tab. 2).

				I	ı	Γ	ı	ı	Γ	Γ	ı	
5	Tab. 2: Gene probes with SEQ ID NOs, function, gi numbers and primer sequences. E. coli gene probes (1-31), P. aeruginosa gene probes (32-80), S. aureus ge	Primer reverse [SEQ ID NO]	ATCCGCCAGTTGCTT AAC [1234]	GGCAATAGCTTTCAC CAG [1270]	CAATAGCTTTCACCA GGG [1268]	AAGTTTAGCCACAGC AGG [1238]	CTGACGTTGGGTATC TCG [1243]	AATCTTCCCTGCTGA AATG [1245]	AATTTCTAATGCAGC GTATTG [1247]	CATCAGCCACAGTTT CAAG [1231]	CCGAGATCGACAACA GAG [1253]	AGAGAGCACCGTC ACTAC [1235]
15	), P. aeruginosa gene probes (	Primer forward [SEQ ID NO]	AGCCTGGTGACGA CTTATC [1233]	TGTTTCTGCACTCG AAATG [1269]	TGTTTGAGGTCACT TTCTGG [1267]	ATGGAATTGCGTCT GTTC [1237]	GACTCGGTACAGC GATTG [1242]	CTTTACGACGGTTC TCCC [1244]	TTGAAACTTCTTAC TGCCG [1246]	GTTTGGGACTTATT GCTCTG [1230]	GAATACCAAAGCA GATCGTC [1252]	ACCACGACAGGTC TTTATG [1234]
<i>25 30</i>	es. <i>E. coli</i> gene probes (1-31) (81-120).	gene probe SEQ ID NO	143	161	160	145	148	149	150	142	153	144
35	nd primer sequence: (8	gi number	453286	145916	145916	16127994	16127994	16127994	16127994	16127994	16127994	8071787
40 45	IOs, function, gi numbers a	Function	Inner membrane osmosensor	Enterochelin esterase (siderophore)	Enterochelin esterase (siderophore)	Bacteriophage N4 receptor, inner membrane protein	Putative membrane protein	Putative enzyme	Putative outer membrane protein		Putative outer membrane protein	Flagellar H antigen
50	robes with SEQ ID N	Symbol	envZ os	fes(2) (si	fes(1) (si	nfrB re-	yacH pr	yagX	ycdS pr	b1169	b1202 pr	fliCb
55	Tab. 2: Gene p	Array No.	-	Ø	ю	4	5	9	7	8	6	10

5		Primer reverse [SEQ ID NO]	AGTCGTCCTGCA TTAC [1277]	CACTTTGCTCCCAGA AATAC [1279]	AGACACCATCCTGCC TTC [1281]	AAGATTCACCATAGA GGCG [1283]	GACACGGAAACCAA ATTAAC [1249]	TGTTGGGTTGAAAGA GTAGC [1251]	CTTGTCATCGGTCAT GTTG [1255]	TTTCCATACTGATTG CCG [1257]	ATCGAAATTGTTACT GGCG [1259]
15 20		Primer forward [SEQ ID NO]	CATCAGGCAGTTAT CCTGTC [1276]	TTCACAGCGGATAT GGAC [1278]	AGACTGGGATTTG GTCAAC [1280]	GGAGTATATTGCGT GGGTAG [1282]	ATAGCAGGCTGT TTGTATC [1248]	TATTGTCATCGCGC AGAG [1250]	CTAACTCATTGTGG TGGAGC [1254]	GGCGTTACTATCCT CTCTATG [1256]	TTTGTTGTTATTGG TACTTCATTC [1258]
		Prim	CAT	)	AG.		ATAGC, TTGTA [1248]	TAT AG/	CT/ TG(	аа Стс	TTTGT1 TACTT( [1258]
25	ed)	gene probe SEQ ID NO	165	166	167	168	151	152	154	155	156
30	(continued)	gene									
35	•	gi number	474189	474189	474189	42307	16127994	16127994	145852	145830	2897961
40		Function	synthesis e)	synthesis e)	synthesis e)	pill protein	mbrane	.l protein	Genetic locus necessary for the production of attaching and effacing lesions on tissue culture, OM protein adhesin	subunit B	
45		lη	Aerobactin synthesis (siderophore)	Aerobactin synthesis (siderophore)	Aerobactin synthesis (siderophore)	Adhesin, P-pill protein	Putative membrane protein	Hypothetical prot	Genetic locus necessa for the production of attaching and effacing lesions on tissue cultur OM protein adhesin	Enterotoxin subunit B	Secretion
50		Symbol	iucA	iucB	iucC	papG	yciQ	ymcA	<i>eae</i>	eltB	escR
55		Array No.	11	12	13	14	15	16	17	18	19

5	Primer reverse [SEQ ID NO]	GAATACGTTTAGTTG AGGCG [1261]	TACCATCAGTATCCT TGGC [1263]	CCATACGATTCTGGA CCTC [1265]	TAAACTCCTTCGGTT GAGC [1273]	ACTTAGCACCCAGTT CGAC [1275]	TGTGAGGTCCACTTC TTCC [1289]	CTGGGTCTCCTCATT ACAAG [1291]	GATTCACAGGTACTG GATTTG [1293]	CGAAATGCTTCTCAA GATAGG [2613]	TCTCAGCGATCTGTC TATTTC [2577]
15	Primer forward [SEQ ID NO]	TTACGCTTCCGATC ATAGTAG [1260]	AAGTGAAGAGGTA ATGGCTG [1262]	GATGGTGACTCTAT TGCAGG [1264]	CTTGGAAATGTTGG TAAAGC [1272]	TCAATGCTGAAACT ATAAGGC [1274]	TTCTTCGGTATCCT ATTCCC [1288]	AAATGGCGACAAAT TATACC [1290]	AAGAAGATGTTTAT GGCGG [1292]	GACCGATCACCCTA CGAG [2612]	ACATGGAACTGGAT CTCAAC [2576]
25	(continued)  gene probe SEQ ID NO	157	158	159	163	164	171	172	173	833	815
35	(co	2897961	2897961	1657262	525328	1247757	304950	148027	148261	45769	21464484
40 45	Function	Secretion	Secretion	Protein secreted by enteropathoge nic E. coli	Enterohemorrh agic Escherichia coli hemolysin	Enterohemorrh agic Escherichia coli hemolysin	Shiga-like toxin type II	Subunit A of heat-labile enterotoxin	Verotoxin-2 variant, beta- subunit, shiga-like toxin	aminoglycoside-(3)-N- acetyltransferase	Class A beta-lactamase
50	Symbol	escT Se	es nose	espB en	hiyA Es	hiyB Es	SLTII Sh	Su soxA-LTPA en	VT2va B sul	aacC2 ao	blaTE M-106 CIR
55	Array No.	20	21	22	23	24	25	26	27	28	59

5		Primer reverse [SEQ ID NO]	TAGACTGCGTTGCTC CTC [2615]	AATTCTTGCGGTTTC TTTC [2721]	GAGGATGAGGATGT TGGC [1935]	GCAGGTCGTACCAG GAAG [1937]	TTCAGGTAGAGCTG GAAATG [1939]	CGACGAAGTGGATA TTGG [1929]	ACTTCCTTGCGGTAC TCC [1931]	TAGACCTCCGAAGA GTTGC [1887]	GTCTTGGCATTGAGT TCG [1945]	ATAAGACCCAAATTA ACGGC [1889]
15 20		Primer forward [SEQ ID NO]	AAGTTTCATTGCCA GACG [2614]	CATCGTCAACATAA CCTCG [2720]	CACTTTCCGTTATT GCCTC [1934]	GACTGGCTGAATC GTCTC [1936]	ATTGTCGATGACGA ACCTC [1938]	CATTGAAAGGTCGT AGCG [1928]	GGTCAAGCACATC CTAGTG [1930]	CAAGCACAACAAG AAATACG [1886]	CTGGGACGTTAGT GTCATC [1944]	GAGCGACCTTGGA TTCTC [1888]
25 30	(continued)	gene probe SEQ ID NO	834	887	494	495	496	491	492	470	499	471
35	))	gi number	17129524	17129524	150990	150999	151003	45279	45279	1399486	309873	151325
40 45		Function	Streptomycin resistance protein B	Dihydropteroate synthase, sulfonamide resistance	Alginate biosynthesis (exopolysacch aride)	Alginate biosynthesis (exopolysaccharide)	Alginate biosynthesis (exopolysaccharide)	Alkaline protease	Alkaline protease secretion	Repression of glycerol metabolic enzymes (glp=glycerol-3- phosphate)	Elastase, virulence protein	Transcriptional activator of elastase
50		Symbol	Stre	Sul Dihy	Algir (exo	Algir algN (exo	Algir algR (exo	aprA Alka	Alka aprE secr	Bep meta glpR (glp-	lasRa	lasRb elas
55		Array No.	30	31	32	33	34	35	36	37	38	39

5		Primer reverse [SEQ ID NO]	ACGATTTCCTCCACC TGT [1947]	CGAAATAGTCGTCCA GCC [1949]	GTCTTCACCTCGACA CCC [2725]	AATTCACGGGTTTTC TCG [1953]	CTCAGCTACAGCCAC GAC [1891]	ACATTGATGGTGTCG TCC [1893]	TCCTTGTCCCAGTAG TTACC [1895]	AACGTCCGAGCAGG ATAC [1901]	CCCTTCTGCGAGTAG TGTT [1903]	CAGGAACAGGTGCT CGTAG [1905]	GAGCCGTAGGTGTT ATCG [1909]
15 20		Primer forward [SEQ ID NO]	AAGAAGTCTCTGCT CCCC [1946]	ATGGCAGTTTCAGT GTCG [1948]	CTCGACCCGATCTA CGTC [2724]	GACCTGCTGTTCCA GTTG [1952]	ATGGATGCTCGGG TACTG [1890]	GATCGTCTCTGCCC AGTC [1892]	AGGAGAGAACATG AGTCGC [1894]	AGGCATCCATCGA GCTAC [1900]	GCGAGGAGGTATT CGACA [1902]	AAGGACTTCTGGTC GGTG [1904]	CGAGCACCAATATC GAAC [1908]
20			AAG	AT(	CTC CGC	GA( GTT	ATG	GAT	AGC AGT [189	AGG	GCG	AAG GGT	CGA
25	(continued)	gene probe SEQ ID NO	500	501	688	503	472	473	474	477	478	479	481
30	(cont												
35		gi number	45340	483463	5616092	4545242	1399486	15595198	15595198	15595198	15595198	15595198	15595198
40		ion	acylglycerol	in he active lipase	tance	iin	tein, olism	otein	otein	otein	otein	otein	otein
45		Function	Extracellulartriacylglycerol lipase	Lipophilic protein necessary for the expression of active	Multidrug resistance protein MexA precursor	DnaJ-like protein	Regulatory protein, glycerol metabolism	Hypothetical protein	Hypothetical protein	Hypothetical protein	Hypothetical protein	Hypothetical protein	Hypothetical protein
50		Symbol	lipA	Ндіі	техА	Orf25 2	OrfX	pa026 0	pa0572	pa1046	pa1069	pa1846	pa408 2
55		Array No.	40	41	42	43	44	45	46	47	48	49	50

5		Primer reverse [SEQ ID NO]	GTCGAACAACGCGA ACAG [1955]	AATTTCTGCATCGGG TTC [1957]	TCGGTTCGAGTTCAT AGC [1961]	GATAGACGTTGTCCT TGACC [1963]	CGACTCTTGCGCGTA TTC [1965]	TCGAGCATCATCAGG TAGAC [1917]	CTTGCCGTAGTGATG CAG [1919]	CTCCAGGTCGAGGA AATG [1983]	GGTCCATTGCAGGAT CTC [1987]	CTTGCCTTCCCAGGT ATC [1991]	TGAGGATAGTCCCTT CGC [1921]
15		Primer forward [SEQ ID NO]	CCTGCTCAACACCT TCTATC [1954]	GTTGAAAGGGTTTA CCGAC [1956]	GACTTCGCTGTTCG ACTTC [1960]	GTGTTCCAGGTGTT CGAC [1962]	ACAACCTGGAACA GCAACT [1964]	GAAGTGAACTCCG CCAAG [1916]	TCGAGAAGTCGAT GTTCAAG [1918]	AGTCTGTTGGTATC GGTTTG [1982]	TTCGATTACTACGC CTATGG [1986]	GTGCGCTACAGCT ACACG [1990]	AGACCTACAACAAG GTTTCG [1920]
20		Prime	CCT( TCTA	GTT(	GAC ACT	GTG	ACA/ GCA/	GAA CCA	TCG	AGT( GGT	TTC( CTA <sup>-</sup>	GTG( ACA(	AGA(
25	( <b>þ</b> .	gene probe SEQ ID NO	504	505	507	508	509	485	486	518	520	522	487
30	(continued)	dene											
35	0)	gi number	4325021	5616088	151492	151497	151499	4545246	1621599	452502	1117916	15595198	3249556
40		Function	Necessary for formation of siderophore pyochelin	osynthesis molecular )	se C (heat ′sin)	ic se C	se C	lpy ruvate- ohotransf	ase II, purine	ransferase ıamnolipid t synthesis	regulation	recursor	an and
45		Fun	Necessary for formatio siderophore pyochelin	Phenazine biosynthesis proteins (low molecular weight toxins)	Phospholipase C (heat labile-hemolysin)	Non-hemolytic phospholipase C	Phospholipase C regulation	Phosphoenolpy ruvate- protein phosphotransf erase	AIR carboxylase biosynthesis	Rhamnosyl-transferase involved in rhamnolipid biosu rfactant synthesis	Rhamnolipid regulation	Exotoxin A precursor	DNA helicase
50		Symbol	pchG	PhzA	DTC	picN	plcR	PstP	purK	rhIA	rhIR	toxA	uvrDII
55		Array No.	51	52	53	54	55	56	29	58	59	09	61

	г											
5		Primer reverse [SEQ ID NO]	AATATCTTCATCGCC AGTTG [1923]	TGCAAGGTACTCACC AGC [1927]	GATACTCTGCTGACC TCGC [1941]	CCGTCGTACTGGAA GTTG [1943]	TCTGCCTTTACCCAG GAC [1897]	CTAGTGGCGAAATTG AACAG [1899]	CGTTGCTCCCTCATA CAC [1907]	TTCTCGTAGTAACCC TCGG [1959]	TCAATAGAGCCAGTC ACACC [1911]	CGTAGTTGGCTTTCC AGTT [1913]
15		Primer forward [SEQ ID NO]	ATTCCTCTCTGAAT CGCTG [1922]	TTCAACCTCAACGG 1 ACTG [1926]	CGTTTGGGACAGA TTGAG [1940]	AATGCGATAACCAT CAGC [1942]	AGGAGCAACTGAA GCGAC [1896]	AAGGTTGGCAGGA TCAAC [1898]	TTCCCTAACGAATG CTGTC [1906]	ATGCTCGATAATGC 1 TATTCC [1958]	GCTTTACCTTGATC GAACTG [1910]	TGCCGTGAGTGAA ATCAG [1912]
25	(continued)	gene probe SEQ ID NO	488	490	497	498	475	476	480	506	482	483
35	3)	gi number	695153	45433	13892017	1633044	15595198	15595198	15595198	5616088	18535593	21629637
40 45		Function	Autoinducer synthesis protein	Secretion protein, translocation of exoproteins across outer membrane	Exoenzyme S, secreted toxin	Ferripyoverdine receptor	Hypothetical protein	Hypothetical protein	Hypothetical protein	Phenazine biosynthesis proteins (low molecular weight toxins)	Type IV pilin, involved in twitching motility and attachment	type IV pilin, involved in twitching motility and attachment
50	_	Symbol	t b	S the property of the property	ExoS t	F fpvA	) + ba0625	) + ba0636	pa3866	PhzB pv	T t t	ti ti ti
55		Array No.	62	63	64	92	99	29	89	69	70	71

5		Primer reverse [SEQ ID NO]	GTCCAGAGCTTCTAC CAGAG [1915]	CTCTGCACAAACTCA GGG [1967]	GTAACGAACGCTATC GGG [1971]	AGCACGCCATTCTTT AACTTC [1973]	TGGCATAAGTATTGG CAG [1975]	AGTGGTACTCGAAG GGTTCT [1977]	TGCAATTTCTTCTTAT TGGC [1979]	ACCAAAGAGTGTTGA TAGCC [1981]	GATACTGTGCGGTTG TGA [1985]	TCACGCTCTTCATTT AGTTCT [2549]
15 20		Primer forward [SEQ ID NO]	GGTATCAACCCACT AAAGGTC [1914]	GTCAAGGGTGTTG TCTGC [1966]	CTTCAGTTCCGAGA TGCC [1970]	ATATACGGAAAAAG AGTTTCTTGAG [1972]	TATACGGCTTCAGA CTTTCC [1974]	TCGCCAATAAGAAG AAATTG [1976]	ATCCAGTATATTCC TGCTCG [1978]	ATCGTTCTGGTCTT CCTTG [1980]	AACGCTTTCTCGAT CAGG [1984]	TACAGTCATTTCAC GCAAAC [2548]
<i>25</i> <i>30</i>	(continued)	gene probe SEQ ID NO	484	510	512	513	514	515	516	517	519	801
35	99)	gi number	18535591	1633044	286179	286179	286182	15595198	15595198	836903	452502	4929298
40 45		Function	Pilin biogenesis protein	Pyoverdine synthetase D (siderophore)	PyocinS1, bacteriocin	Immunity protein of pyocin S1	PyocinS2	PyocinS2	PyocinS2	B-band LPS (O-antigen) biosynthesis	Rhamnosyl- transferase involved in rhamnolipid biosurfactant synthesis	Factor essential for methicillin resistance
50		Symbol	PilC	) Opvd	Pyocin S1	pyocin S1im	Pyocin S2	Pys2(1)	Pys2(2)	<i>rbf30</i> 3 b	F in the second	femA n
55		Array No.	72	73	74	75	92	22	82	62	80	81

				I					ı			
5		Primer reverse [SEQ ID NO]	GCTGTTAATTGTTGT TGCTTT [2597]	CTTGCTTTTCAGATG TTTCC [2583]	GGTTTTGAGCACGAT ATGTAG [1067]	AAAAATCGTTCAAAG TGCTC [1069]	TTTTTAACATCTCGA ACTATATCTAA _[1071]	AGACCATGTATGTAG GTGGC [1077]	GTAGCGAAGTCTGG TGAAAA [1187]	GTCATTGTCCTTTGT TGGTT [1083]	GGCTTTGTTGCTTTT AATGA [1085]	TGATGTTAGCCCAAT CTACA [1197]
15 20		Primer forward [SEQ ID NO]	TGACTTCGGATGA GTTCAAT [2596]	CTCACCCAAATGGA GATTTA [2582]	AGGCTCGTATGATT GAAAAA [1066]	TTGGCACAACTGAT AAGACA [1068]	ATCATCAGCGACAA TGAGAG [1070]	TCTTCCATTCTCTC AGTCAAA [1076]	GTCAGCTCAGTAAC AACAACAC [1186]	TGCATCTTCCATTT TAATAGC [1082]	TTGACAGCTTTGCA TTTTTA [1084]	AAGTTGCTCAAATA CAAGCTG [1196]
25 30	(continued)	gene probe SEQ ID NO	825	818	09	61	62	65	120	89	69	125
35	o)	gi number	4574232	4574234	296393	296393	2589180	14349226	46763	393265	1255258	2506026
40 45		Function	Factor essential for methicillin resistance	Factor essential for methicillin resistance, putative	DNA gyrase subunit A	DNA gyrase subunit B	Porphobilinogene synthase	Oxygen-independent coproporphyrin ogen oxidase	lpha-Hemolysin	Lipase	o-Succinyl-benzoic acid synthetase	N-acetyl-glucosaminidase
50		Symbol	fmhA m	finhB m	gyrA	gyrB	Pc hemB sy	(O ) cc	hla α-	lip Li <sub>l</sub>	menC sy	NAG
55		Array No.	82	83	84	85	98	87	88	68	06	91

5		Primer reverse [SEQ ID NO]	CGTAATCGCAATCGA AATA [2755]	GAATCAGCGTTGTCT TCG [1089]	TGGATCAAAGAAACG TGAAT [1093]	CATTCATTTTATTCCC ACCT [1109]	TCAGGCTTTCGCCCA TT [2831]	GTTTTGACCTGAAGC TGTATC [955]	GGCCATTATTGGTCT GTTG [1173]	AGCGTGTCATATCCT TCATC [2739]	GTCAAACGAGTGCTA ATGGT [1063]	TTATCTGTCGGTTTC TCTGG [1065]
10		Primer	CGTA. AATA	GAAT( TCG [	TGGA <sup>-</sup> TGAA1	CATTC ACCT	TCAGGCT TT [2831]	GTTTT TGTA1	GGCC	AGCG TCATC	GTCA/ ATGG1	TTATC TCTGC
15		Primer forward [SEQ ID NO]	GGTTACTTGTTGCT GCTTTT [2754]	TGGCTATCAGTAAT GTTTCG [1088]	CATCGT [1092]	TTTTGATTTATCTTC TGACGG [1108]	TCTCTGATGTTAGC GGCGG [2830]	TAGCATAGCAACAA ACAGTGA [954]	AAAGATAGTTCTAA GATAAATGGTC [1172]	ATTAGAAATTGCGA CTGGTG [2738]	CTTAGATGTCCCAT GCTGAT [1062]	TTCAATAGGCGTG GTGTC [1064]
20		Primer forwa	GGTTACTTGTT GCTTTT [2754]	TGGCTATCAGT GTTTCG [1088]	TGGAAGACATCGT AAACGTA [1092]	TTTTGATTTATC TGACGG [1108]	TCTCTGATGTT GGCGG [2830]	TAGCATAGCAAC ACAGTGA [954]	AAAGATAGTTC1 GATAAATGGTC [1172]	ATTAGAAATTGC CTGGTG [2738]	CTTAGATGTCCC GCTGAT [1062]	TTCAATAGGC GTGTC [1064]
25		gene probe SEQ ID NO	904	71	73	81	942	4	113	968	58	59
30	(continued)	geneprol										
35	)	gi number	4115706	46623	677848	6434027	46498	3393010	152997	1841513	21204850	153019
40		Function	sistance		rase B-	ıyladenine		ctor B	ell n inhibitor	oilancin K7	Biosynthesis of lantibiotic epidermin; serine protease	ırsor; glycerol lase
45		Fur	Quinolone resistance protein	Nuclease	RNA polymerase B- subunit	DNA- 3-methyladenine glycosidase	16S rRNA	Clumping factor B	Epidermal cell differentiation inhibitor	Lantibiotic epilancin tranlocator	Biosynthesis epidermin; s	Lipase precursor; gl ester hyderolase
50		Symbol	norA2 3	nnc	гроВ	tag	16SSa	clfB	EDIN	elkT-abcA	epiP-bsaP	geh
55		Array No.	92	93	94	95	96	26	86	66	100	101

5		Primer reverse [SEQ ID NO]	ATCGACAAAACGTAC AGGAT [2761]	GGATATTTCTTTCGT GCTGT [1087]	ATGCTCTGATAAATC TGGGA [1199]	TTTTCAGAGTTAATC GTTTTATTATC [1201]	CTTTTATGTCTAGTT CTTGAGCTG [1205]	CTGATCCAGAGTTTC CTACCT [1177]	CTTGAGCAGTCACCT TTTTC [1203]	TGACAATCGCTTTAT TCATTT [1107]	CAATAACCACCGTT TTATC [1223]	TGTTGCATTTAGTCT TTCCA [2633]
15 20		Primer forward [SEQ ID NO]	TACGATGACACCA GTCTTTG [2760]	GTATTATTGCTTGG GGTGAT [1086]	TGTTATTATTCTCA TTTTCTTCAAT [1198]	TTTTATTCATTGCC CTAACG [1200]	AATTTTTGGCACAT GATTTA [1204]	TTTTAGCAGCGTCA ATTTTT [1176]	CGTAGATGTGTTTG GAGCTA [1202]	TGATATTGGAAGAT ATTAGCATAGA [1106]	TTTTATCGTAAGC CCTTTG [1222]	AGATTTGCCAGAAC ATGAAT [2632]
25 30	(continued)	gene probe SEQ ID NO	206	02	126	127	129	115	128	80	138	843
35	0)	gi number	7548683	2642658	47425	153120	46566	15301	152999	3724154	18266750	3676412
40		Function	ABC transporter	UDP-N-acetylmuramoyl- L-alanine synthetase	Staphylokinase	oxin A	oxin C	Exfoliative toxine B precursor	oxin B	Iron transport protein	Toxic shock syndrome toxin	Bifunctional aminoglycoside modifying enzyme
45			ABC tra	UDP-N L-alanit	Staphy	Enterotoxin A	Enterotoxin C	Exfoliative precursor	Enterotoxin B	Iron tra	Toxic s toxin	Bifunctional aminoglycos enzyme
50		Symbol	mreA	murC	sak	sea	sec1	etb	ges	sstC	tst	aacA-aphD
55		Array No.	102	103	104	105	106	107	108	109	110	11

55	50	40 45	35	25 30	15 20	5
			9)	(continued)		
Array No.	Symbol	Function	gi number	gene probe SEQ ID NO	Primer forward [SEQ ID NO]	Primer reverse [SEQ ID NO]
112	aadD	Aminoglycoside acetyl transferase	21623792	837	GCTATTGGTGTTTA TGGCTC [2620]	CTGATTGCTTAACTG CTTCA [2621]
113	aph-A3	3'5'-aminoglycoside acetyl-transferase	1272325	840	GAGAATATCACCG GAATTGA [2626]	GCTCGACATACTGTT CTTCC [2627]
114	blaZ	β-lactam ase	1575124	827	TGCTTTAGTTTTAA GTGCATGT [2600]	TCCTTCATTACACTC TTGGC [2601]
115	cat	Chloramphenicol acetyl- transferase	46651	862	AGAAAATTGGGATA GAAAAGAA [2670]	CTGCAAGGCAACTG GTAT [2671]
116	dfrA	S1 dihydrofolate reductase	3676404	859	CAATTACCTTGGCA CTTACC [2664]	CCCTTTTCTACGCAC TAAAT [2665]
117	ermA	rRNA methylase	13785452	852	CCAGAAAAACCCTA AAGACA [2650]	AAAGAACACGATATT CACGG [2651]
118	ermC	Adenine methylase	4138444	846	ACACAGTCAAAACT TTATTACTTCA [2638]	CAACAAGTTTATTTT CTGTAGTTT [2639]
119	msrSA	Macrolide antibiotic resistance	3892641	854	GACAGATTTTCGAT CCCTTA [2654]	CCTTTTTGTTTTGAT GCACT [2655]
120	тесА	Penicillin binding protein 2'	13785452	802	AGTTGTAGTTGTCG GGTTTG [2550]	TGAAGTCGCTTTTCC TAGAG [2551]

[0098] S. aureus, E. coli and P. aeruginosa genes were selected from the literature and databases, and compared by BLAST analysis to all other sequences available in the NCBI database. Primers were designed to amplify gene segments of 200-810 bp length and devoid of apparent homology with genes of other bacterial species and Homo sapiens. Gene segments were amplified by using the puReTaq Ready-To-Go PCR beads (Amersham Biosciences, Freiburg, Germany) and cloned into the pDrive Cloning Vector (Qiagen, Hilden, Germany) according to the recommendations of the suppliers and transformed into competent Escherichia coli (XL-1-Blue) cells using the calcium chloride protocol (Sambrook, J., Russel D.W., Molecular Cloning: A Laboratory Manual. Cold Spring Harbor Laboratory Press, NY (2001)).

**[0099]** For quality control purposes, all gene probes were partially sequenced and verified (with the BigDye kit 1.1 and an 377 DNA sequencer; Applied Biosystems, Foster City, USA). All sequences obtained were identical or substantially identical (>90% sequence identity) to those obtained from the database.

**[0100]** For DNA-probe production 120 recombinant plasmids containing *S. aureus, E. coli* and *P. aeruginosa* gene segments were used for re-amplification. Amplicons were purified and spotted in 4 replicates per slide on UltraGAPS<sup>™</sup> Coated Slides (gamma amino propyl silane coated slides, Corning, NY, USA). Approximately 1 nl DNA (with a concentration of about 0.1 to about 0.2 ng/nl) per spot was spotted onto the slide with a Biorobotics Microgrid Microarrayer (Genomic Solutions, Ann Arbor, MI, USA).

### Example 5: Hybridisation and scanning

[0101] All experiments described represent dual co-hybridisations of two different target DNA samples labelled respectively with Cy3, Cy5 or Alexa647. After removal of unbound label, Cy3 and Cy5/Alexa647 labelled DNAs were pooled and mixed with 10 μg of Salmon Sperm DNA and 50 μg of poly-A-DNA. The mixture was frozen in liquid nitrogen and lyophilised in the dark. Prior to hybridisation the target DNA was reconstituted in 33 μl H<sub>2</sub>O and 55 μl 2x hybridisation solution (Memorec Biotec GmbH, Cologne, Germany) and chemically denatured with 11 μl denaturation buffer D1 (Mirus) and neutralized with 11 μl buffer N1 (Mirus) according the instructions of the supplier. Hybridisation was automatically performed with a TECAN Hybridisation Station (HS400, TECAN, Salzburg, Austria). The arrays were prewashed at 60 °C for 1 min with 0.2% SDS and 4x SSC and prehybridised in 120 μl denatured prehybridisation buffer (Memorec) for 30 min at 60 °C at mild agitation. After injection of 110 μl labelled DNA, hybridisation was performed at 60 °C for 18 hours at mild agitation. The arrays were washed at 50 °C in primary wash buffer (Memorec) - five cycles of 1 min wash time and 30 s soak time - and in secondary wash buffer (Memorec) - five cycles of 20 s wash time and 30 s soak time -, and finally dried at 30 °C with N<sub>2</sub> (2.7 bar) for 3 min. Hybridised arrays were scanned with a Scan Array 5000 laser scanner (PerkinElmer). Laser light of wavelengths at 532 and 635 nm was used to excite Cy3 dye and Cy5/Alexa647 dye, respectively. Fluorescent images were analysed by the ImaGene software (BioDiscovery, El Segundo, CA, USA).

### 35 Example 6: Specificity

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**[0102]** In order to allow the simultaneous and rapid identification of *S. aureus*, *E. coli* and *P. aeruginosa* grown in blood culture specimens from septicemic patients, a microarray comprising a set of 40 *S. aureus*, 31 *E. coli* and 49 *P. aeruginosa* gene probes of 200 to 810 bp length was developed (Tab. 2).

[0103] The specificity of the DNA-chip was validated firstly (compare Example 1) with 45 well characterised clinical isolates and reference strains of the three target species as well as other related bacteria and secondly (compare Example 2) with 13 blood cultures from sepsis patients.

**[0104]** In all assays, three PCR-amplified DNA-segments, which had been added to each DNA preparation as a positive control, hybridised with the corresponding probes, indicating that labelling and hybridisation had performed efficiently.

**[0105]** Hybridisation experiments with *S. aureus*, *E. coli* and *P. aeruginosa* target DNAs, respectively, revealed specific hybridisation with the species-specific gene probes (Fig. 1). There was no cross-hybridisation between the three species with the exception of the *S. aureus* 16S rRNA gene probe (16SSa, Fig. 1 C), which hybridised also with *E. coli* and *P. aeruginosa* target DNA.

[0106] Identification of *E. coli, P. aeruginosa* and *S. aureus* reference strains, clinical isolates and blood cultures (BC) by m icroarray analysis corresponded by 100% with the conventional identification results (Fig. 1).

#### Example 7: Detection and discrimination

### 55 Example 7A: Detection and discrimination of E. coli

[0107] All DNA samples from 9 *E. coli* strains hybridised always with seven *E. coli* gene probes (*envZ*, *fes* (1) and (2), *nfrB*, *yacH*, *yagX*, *ycdS*) (Fig. 1 A, columns 19 to 27); in the following these genes are designated as core genes.

With 14 *E. coli* gene probes variable hybridisation was observed including the antibiotic resistance gene probes *bla-TEM106*, *sul*, *strB* and *aacC2*. Such a variable hybridisation profile is expected for antibiotic resistance genes since acquired resistance to antimicrobials is strain specific. For 11 *E. coli* virulence gene probes *(eae, eltB, escR, escT, escU, espB, hlyA, hlyB, SLTII, toxA-LTPA, VT2vaB)* no hybridisation signals were detected with any of the tested *E. coli* isolates and blood cultures. Since these virulence genes are known to be specific for particular *E. coli* pathotypes (Bekal, S. et al., J. Clin. Microbiol., 41:2113-25 (2003)), it was not surprising that they were not present in the tested strains. The *eae, esc* and *esp* genes for example are encoded on a chromosomal pathogenicity island, which is typical for enteropathogenic *E. coli* exhibiting the unique virulence mechanism known as attaching and effacing (AE) (Elliott, S.J. et al., Mol. Microbiol., 28:1-4 (1998)). The alpha-hemolysin *(hly)* operon is encoded on a large plasmid of enterohemorrhagic *E. coli* strains (Schmidt, H. et al., Infect. Immun. 63:1055-61 (1995)).

### Example 7B: Detection and discrimination of Pseudomonas aeruginosa

**[0108]** DNA samples obtained from *P. aeruginosa* uniform ly hybridised with 32 out of 49 *P. aeruginosa* specific gene segments including the *mexA* gene probe (core genes). Variable hybridisation was observed with 17 probes allowing for discrimination of individual *P. aeruginosa* isolates (Fig. 1 B, columns 12 to 18).

### Example 7C: Detection and discrimination of S. aureus

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[0109] Hybridisation experiments performed with 11 *S. aureus* target DNAs revealed signals in all assays with 16 *S. aureus* gene segments (core genes) (Fig. 1C, columns 1 to 11). Variable hybridisation was observed with 14 *S. aureus* gene probes including the 6 antibiotic resistance gene segments *aadD*, *aacA-aphD*, *blaZ*, *dfrA*, *ermA* and *mecA* and the virulence genes *sak*, *sea*, *sec1* and *EDIN*. The gene probes *geh*, *mreA*, *clfB* and *elkT-abcA* hybridised with 8, 10 (*mreA* and *clfB*) and 6 target DNAs respectively. However, PCR am plification of the four genes was positive for all 11 *S. aureus* target DNAs (not shown) suggesting that the four genes were present in all strains investigated and that these gene probes did not allow reliable detection of the four genes in *S. aureus*.

**[0110]** No hybridisation was observed with 10 probes including the toxin genes *seb*, *tst* and *etb*. In contrast to the community-acquired, multi-susceptible MRSA strain MW2 that hybridised to *mecA* and *blaZ* only, all six clinical MRSA strains showed the same multiresistant hybridisation pattern and their DNA hybridised to *ermA* (erythromycin resistance), *mecA* (oxacillin resistance) and the *aadD* gene (tobramycin resistance). As for the majority of multiresistant MRSA strains the *ermA* and *aadD* genes were shown to be located upstream and downstream, respectively, of the *mecA* gene in the mec chromosomal region (Chambers, H.F., Clin. Microbiol. Rev., 10:781-91 (1997); Polyzou, A. et al., J. Antimicrob. Chemother., 48:231-4 (2001)). Hybridisation to the core gene probes permitted the identification of *S. aureus*, while hybridisation to antibiotic resistance gene probes allowed for discrimination of strains.

#### Example 7D: Discrimination of E. coli. P. aeruginosa and S. aureus from related bacterial species

**[0111]** Co-hybridisation experiments performed with related bacterial species confirmed the high specificity of the DNA-chip (Fig. 1): For *S. epidermidis* and all other Coagulase-negative staphylococci, cross-hybridisation was observed only with the *S. aureus* 16S rRNA gene probe (16SSa, Fig. 1 C) and several common staphylococcal antibiotic resistance determinants (*aadD, aacA-aphD, aph-A3, blaZ, cat, dfrA, ermA, ermC, mdrSA, mecA*) (Fig. 1C, columns 28 to 36). There was no cross-hybridisation with other metabolic or virulence genes of *S. aureus*.

[0112] The *Micrococcus* spp. isolate showed no hybridisation with the DNA-chip (column 53). Streptococci (column 56 to 58) and enterococci (columns 54 and 55) showed hybridisation with the staphylococcal 16S RNA gene probe and once with the staphylococcal *aph-A3* aminoglycoside resistance gene probe (*Enterococcus* spp.) (Fig. 1C). Out of 12 strains of seven Gram-negative species (columns 41 to 52), two hybridised with the *S. aureus* 16S rRNA gene probe (*Klebsiella pneumoniae* and *Proteus mirabilis*, Fig. 1C, columns 41 and 47) and one clinical isolate of *Proteus mirabilis* hybridised with the *E. coli* resistance genes *bla-TEM106* (β-lactam resistance), *sul* (sulfonamide resistance) and *strB* (streptomycin resistance) (Fig. 1A, column 42). *Serratia, Stenotrophomonas, Acinetobacter* and *Enterobacter* species showed no cross-hybridisation with any gene probe.

### Example 8: Sensitivity

**[0113]** While the majority of *P. aeruginosa* probes allowed unambiguous identification, some probes showed variable hybridisation patterns when microarray hybridisation was performed with different target DNA samples prepared from the same isolate (Tab. 3).

Tab. 3: Microarray hybridisation signals obtained with different target DNA preparations of *Pseudomonas aeruginosa* isolates.

		C4242		Isol C3	ate 8853	C3	045	C3	755
DNA amount [ng]	130 <sup>a</sup>	382 <sup>a</sup>	1350 <sup>b</sup>	510 <sup>a</sup>	> 2400 <sup>b</sup>	550 <sup>a</sup>	2950 <sup>b</sup>	1180 <sup>b</sup>	> 1600 <sup>b</sup>
BDRº	22	75	48	29	30	90	41	139	40
No. of hybridised gene probes <sup>d</sup>	38 (88%)	31 (72%)	43 (100%)	36 (88%)	41 (100%)	34 (89%)	38 (100%)	41 (95%)	43 (100%)

a Labelled with Alexa647

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[0114] Successful hybridisation with strong fluorescent signals depends on efficiency of DNA labelling (ratio of bases per one dye molecule) and amount of labelled DNA. For the different target DNA preparations of four clinical isolates, variable hybridisation was observed with 14 gene probes (*uvrDII*, *vsmI*, *pa1069*, *rhIR*, *rhIA*, *rhIB*, *1046*, *pyocinS*, *pyocinS1im*, *plcR*, *plcN*, *PHZb*, *rbf303* and *plIAp2*). For example, for three different DNA preparations of isolate C4242, hybridisation to *Pseudomonas*-gene probes varied from 31 to 43 probes, respectively, depending on the labelling efficiency and amount of DNA (Tab. 3). The lowest number of signals was detected with 382 ng target DNA, that, however, showed a high base to dye ratio of 75. Overall, the results suggest that varying amounts of DNA and base to dye ratios influenced the hybridisation results of few gene probes. However, irrespective of the varying quality and quantity of the labelled target DNA, 35 of the 49 *P. aeruginosa* gene probes showed robust hybridisation results in all performed experiments.

### Example 9: Detection and characterisation of pathogens in blood cultures

[0115] Although DNA prepared from blood cultures comprises a mixture of human and bacterial DNA, the resulting hybridisation signals obtained with DNA from 1 ml positive blood culture allowed a clear and unambiguous characterisation of *S. aureus*, *E. coli* and *P. aeruginosa* present in 13 tested blood specimens (Fig. 1). In accordance to the VITEK2 characterisation, positive BACTEC® cultures were identified by microarray hybridisation as multi-resistant MRSA (Fig. 1C, column 8), penicillin-resistant *S. aureus* (column 9 and 11), multi-susceptible *S. aureus* (column 10), *E. coli* (Fig. 1A, columns 26 and 27), *P. aeruginosa* (Fig. 1B, column18), and discriminated from oxacillin resistant *Staphylococcus epidermidis* (columns 33-35), *Proteus mirabilis* (column 43) and *Streptococcus pneumoniae* (columns 57 and 58).

Example 10: Correlation between susceptibility testing and microarray hybridisation of selected antibiotic resistance genes

**[0116]** <u>S. aureus:</u> For 11 Staphylococcus aureus strains and blood cultures, susceptibility results determined by the VITEK2 system, Etest strips and disk diffusion tests were compared with the results of the m icroarray hybridisation assay for the simultaneous detection of antibiotic resistance genes (Tab. 4). The presence or absence of resistance genes as indicated by microarray hybridisation was confirmed by PCR with gene specific primers (results not shown).

Tab. 4: Correlation between phenotypic and genotypic antibiotic resistance for 11 *S. aureus* isolates and blood cultures.

a) Penicillin resistance <sup>a</sup>	Hybridisation with mecA/blaZ					
	No. pos.	No. neg.				
10 (resistant)	10	0				
1 (susceptible)	0	1				

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b Labelled with Cy3 or Cy5

<sup>&</sup>lt;sup>c</sup> BDR: Base to dye ratio; number of nucleotides per one dye molecule

<sup>&</sup>lt;sup>d</sup> Number of signals obtained with *P. aeruginosa* capture probes (total 49) after hybridisation with different DNA preparations. The percentage of specific hybridisations is compared to the highest number of signals obtained for each isolate (100%).

(continued)

b) Oxa	cillin resistance	Hybridisation	with mecA
		No. pos.	No. neg.
	7 (resistant)	7	0
	4 (susceptible)	0	4
c) Erytl	nromycin resistance	Hybridisation with <i>ern</i>	nA, ermC or msrA
		No. pos.	No. neg.
	6 (resistant)	6	0
	5 (susceptible)	0	5
d) Tobi	ramycin resistance	Hybridisation	with <i>aadD</i>
		No. pos.	No. neg.
	5 (resistant)	5	0
	6 (susceptible)	0	6
e) Gen	tamicin resistance	Hybridisation wit	h aacA-aphD
		No. pos.	No. neg.
	0 (resistant)	0	0
	11 (susceptible)	0	11
f) Trime	ethoprim resistance	Hybridisation	with dfrA
		No. pos.	No. neg.
	1 (resistant)	0	1 <sup>b</sup>
	10 (susceptible)	0	10

b dfrA gene detected by PCR

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[0117] For the *S. aureus* strains there was a 100% correlation between phenotypic resistance to penicillin and hybridisation to the *mecA* and/or *blaZ gene* (both genes confer resistance to penicillin, Tab. 4a). Phenotypic resistance to oxacillin correlated 100% with the hybridisation of the *mecA* gene (Table 4b), between resistance to erythromycin and hybridisation to the erythromycin resistance genes *ermA*, *ermC* or *msrSA* (Tab. 4c) and between resistance to tobramycin and hybridisation to the *aadD* gene (Tab. 4d). Furthermore, they all showed 100% correlation between phenotypic susceptibility to gentamicin and no hybridisation to the resistance genes *aacA-aphD* (Tab. 4e). Notably the *dfrA* gene of the trimethoprim resistant strain MW2 (MIC of 1 µg/ml) was not detected by microarray hybridisation (Tab. 4f), whereas PCR amplification revealed the presence of the *dfrA* gene.

**[0118]** <u>E. coli</u> and other Gram negative bacteria: The prototype microarray harboured only four *E. coli* and one *P. aeruginosa* resistance gene probes which do not yet allow a comprehensive prediction of antibiotic resistances. Nevertheless, hybridisation with the *E. coli* resistance gene probe *blaTEM106* was observed in one *P. mirabilis* and four *E. coli* strains and correlated with phenotypic ampicillin resistance for all five strains (Tab. 5).

<u>Tab. 5:</u> Correlation between ampicillin/penicillin resistance, gentamicin/tobramycin resistance and streptomycin resistance and hybridisation with the resistance gene probes *blaTEM-106*, *aacC2*, *aph-A3* and *strB*, respectively.

45	Species	Resistance		Hybridis	sation with	
		phenotype <sup>a</sup>	blaTEM-106 <sup>b</sup>	aacC2 <sup>b</sup>	aph-A3 <sup>c</sup>	strB <sup>b</sup>
	E. coli ATCC 25922	susceptible	-	-	-	-
50	E. coli C4821	AMP, STR	+	-	-	+
	E. coli F3437	AMP	+	-	-	-
	E. coli C3941	AMP, STR	+	-	-	+
55	E. coli F1806 <sup>d</sup>	AMP, GEN, TOB, STR	+	+	+	+
00	E. coli C4547	AMPi	-	-	-	-
	E. coli C4230	AMP	-	-	-	-

(continued)

	Species	Resistance	Hybridisation with							
		phenotype <sup>a</sup>	blaTEM-106 <sup>b</sup>	aacC2 <sup>b</sup>	aph-A3c	strB <sup>b</sup>				
5	E. coli C3940	susceptible	-	-	-	-				
	E. coli F1642d	STR	=	-	-	+				
	<i>P. mirabilis</i> C4024	AMP, STR	+	-	-	+				
10	<i>P. mirabilis</i> C4403	susceptible	-	-	-	-				
	<i>P. mirabilis</i> F1738	susceptible	-	-	-	-				

- <sup>a</sup> AMP, ampicillin; GEN, gentamicin; STR, streptomycin; TOB, tobramycin; i, intermediate
- b E. coli gene probes

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- <sup>c</sup> S. aureus gene probes
- d Positive blood culture

**[0119]** One *E. coli* blood culture showed also resistance to tobramycin and gentamicin. This phenotypic resistance correlated with the hybridisation of the *aacC2* gene probe for am inoglycoside resistance and the *S. aureus aph-A3* probe for tobramycin/kanamycin resistance (Tab. 5). For one *P. mirabilis* and four *E. coli* strains, phenotypic resistance to streptomycin correlated with hybridisation to the *strB* probe (Tab. 5).

**[0120]** All *P. aeruginosa* strains hybridised with the *mexA* gene probe (Fig. 1) and showed phenotypic resistance to tetracycline, trimethoprim/sulfamehoxazole, penicillins (ampicillin, mezlocillin) and cephalosporines (cefazolin, cefixime, cefuroxime). The *mexA-mexB-oprM* operon is a determinant for a three component efflux system responsible for intrinsic and acquired multiresistance in *P. aeruginosa* (β-lactams, fluoroquinolones, trimethoprim, sulphonamides, chloramphenicol and others) (Poole, K., Clin. Microbiol. Infect. 10:12-26 (2004)).

### Example 11: Microarray for specific detection of S. aureus

### A) Strains and Cultures

[0121] Reference strains and clinical isolates: The following bacteria were purchased from the American Type Culture Collection (ATCC, Manassas, Va.) or the Deutsche Sammlung für Mikroorganismen und Zellkulturen (DMSZ, Braunschweig, Germany) and were used for evaluation of the specificity of the microarray: *Staphylococcus aureus* (ATCC 29213), *Staphylococcus epidermidis* (ATCC 12228; ATCC 18610) *Staphylococcus saprophyticus* (ATCC 14953), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853). Ten clinical MRSA (methicillin resistant *S. aureus*) isolates were obtained from the inventors' clinical routine microbiology laboratory.

[0122] <u>Bacterial cultures:</u> Bacterial strains and clinical isolates were plated either onto sheep blood or onto Mueller-Hinton agar from 50% glycerol stocks. One colony was then picked and transferred to 5 ml Luria-Bertani (LB) broth and cultured overnight at 37°C.

[0123] Blood cultures: Aerobic blood culture bottles (BACTEC® Plus aerobic, Becton Dickinson, Heidelberg, Germany) were inoculated with 100 CFU of *S. aureus* after adding 10 ml blood from healthy volunteers. A BACTEC® 9240 blood culture system (Becton Dickinson) - a continuous reading, automated, and computed system detecting the growth of microorganisms by monitoring CO<sub>2</sub> production - was used for incubation according to the manufacturer's recommendations. Bottles with a positive growth index were removed from the incubator, and an aliquot of 1 ml of the blood culture suspension was taken aseptically with a needle syringe. The aliquot was equally divided, with one part for subculture on agar plates and CFU determination, and one part for DNA isolation.

[0124] Additionally, in order to test the microarray upon real conditions, samples were collected from ten clinical positive blood culture specimens cultivated under the same conditions as described above. Six of them were positive for different *S. aureus* strains and four for other bacterial species (*Staphylococcus epidermidis*, *Streptococcus mitis*, *E. coli* and *Klebsiella oxytoca*). Blood culture aliquots of 500 µl were used for DNA preparation.

#### B) Generation of the S. aureus specific microarray

[0125] About 140 gene segments of *S. aureus* genes, but also a few of CoNS (SEQ I D NO: 177,178,179), were selected from the literature and nucleotide databases in order to cover different functional categories (virulence factors,

species-specific metabolic and structural features, antibiotic resistance determinants). Tab. 6 provides the complete list

	of selected genes with gene symbol, gene function and SEQ ID NO of the segments.
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<i>35</i> 40	
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Primer reverse [SEQ ID NO] GTCATTACATCAACTT TATTCCGATTATTAGGCG TTCAAAGTTTTCGTATGTT CACGTCTAACCGCTTTAC GCTATTCTTCCATCTAATT TGGAACTAATTCTCCTTC ATTACACCATTAACGATA CAAATGATTTATTGCCGT TTATATTGCGTTTCAAGA 5 FACGATCATA [1113] GCATGTTA [1143] ATTGGCAT [1139] GATTGTTA [1137] CTCCTA [1141] FGATTG [961] GCTGC [1145] Tab. 6: Selected S. aureus genes, selected segments (SEQ ID NO) and primers used for segment amplification (SEQ ID NO) TAG [1115] TCA [949] 10 15 Primer forward [SEQ ID NO] **ACCTTCAATATTCGCA** ATGAGATACCTAACAT GTTATCAATTAATACA AGACTTATTATCTAAA **TAAATTGTTTAGATTA** AATGCTGCTAACCTG AGCTGAGACGACACA GTAGTTGAAAATATG **AAAATTGCTGGTATC** CAATCAGAGG [948] CGTGGTGAACTAGC AGATCAAA [1144] CAGGAGAATCA [1112] GCTGCA [1142] **ACCCCTGAAGC CCTGTTGGTGT** CGTGAT [960] 20 TCC [1114] [1140] [1136] [1138] 25 gene probe SEQ ID NO 30 66 84 83 95 96 97 86 / 35 3-phosphoshikimate 1-carboxyvinyl-transferase 3-deoxy-D-arabino-heptulosonate-7-phosphate synthase 40 Functions Shikimatdehydrogen ase 45 alkaline shock protein Chorismatsynthase Chorismat-Mutase endopeptidase autolysin 50 catalase Gene symbol 55 asp23 aroC aroE aroF aroG aroA clpCcata atl

5	Primer reverse [SEO ID NO]		ATTCAAGC 3]	ттеттес	TTTAGCTC	3AACCATT	TACTTTGT [971]	TAATGCTT 73]	CCTTTTACT	CATAAATA 7]	AGCAGTT 21]	ATGGTACA
10	Drimer reverse		ACCTAATAAAATTCAAGC ATTGGGA [963]	ACGTAATCGTTTTGTTGC CAAATA [965]	TTGCGTTTCTATTTAGCTC AGACA [967]	GACCTTGAATGAACCATT GACCAT [969]	CCTAACCATGTACTTTGT AACACTTTCA [971]	CTGAACTCTTCTAATGCTT CAACGATT [973]	TTTGTCGTCGTCTTTTACT TCGTT [975]	GAGCGTATCGCATAAATA ATCTTTTC [977]	GGTGTTACTAAAGCAGTT GAAAACG [1121]	CCTCTTGAAGATGGTACA CGGAT [981]
15	5	<u>_</u>	1 <b>.</b>		L	(5	O	A	T		G	<u> </u>
20	Primer forward [SEO ID NO]	ופו וסושמוט ier וטושמוט ier	AAAGTAAAGAGTAGA CTAAGCTGTCTGCTC [962]	AAGAATTTAAAATGGT TAGGTGTCGTA [964]	AACGTCCCATGCCATT AATTTT [966]	ACAGAGCAGCAAAAG CGTTAGTG [968]	CATATGGTGATTTTAC ATTCTTCTTAATTG [970]	AAATTTATTAGCAGAA GTAGCAGAAAATG [972]	TTTAGGCGAAAATATT GGTGAAGA [974]	GGTCTTATCGTTGCA GCTATCACTAT [976]	CGATGTTCATCATTGC TACTGGTA [1120]	TAGTCACCATGAAGTT GCCCC [980]
25	Dring	<u>_</u>	AAAG CTAA( [962]	AAG TAG	AAC	ACA CGT	CATA ATTC [970]	AAATI GTAG [972]	TTT	GGT	CG/ TAC	TAG
30	(continued)	gerie probe SEG ID NO	&	6	10	11	12	13	14	15	87	17
35												<u>S</u>
40	ų	2			s III stress genes	tein ligase	ısporter			cator	jenase	glutamine synthetase; belongs to the fem C locus
45	Finotions	Laricilor		osynthesis	transcription repressor of class III st homologue	D-alanine-D-alanyl carrier protein ligase	hypothethecal membrane transporter	r protein	otein	lantibiotic epilancin K7 translocator	2-phosphoglycerate dehydrogenase	:hetase; belong
50			endopeptidase	cytochrome biosynthesis	transcription re homologue	D-alanine-D-a	hypothethecal	D-alanyl carrier protein	Heat-shock-protein	lantibiotic epile	2-phosphoglyc	glutamine synt
55	lodmys energ	Gerie syrriboi	срР	ctaA	ctsR	dltA	dltB	dltC	dnak	elk T	eno	glnA

5		Primer reverse [SEQ ID NO]	TATTGGCA	AGATTTGAA 5]	AAACTTAAAATACTTTCTG AATATTGATCAT [987]	TCGCCTTC	GTTTCATTT	CATCTGCAT 7]	GCATATCC 169]	ATTCCAGA AT [993]	ATTGCTGTT \G	GTGTATGTC A [1073]
10		Primer revers	CACCACGATTTATTGGCA AAGTT [983]	CAGTCGTTCAGATTTGAA TTTCTTT [985]	AAACTTAAAATACTTT( AATATTGATCAT [987]	TGTTAATGCATCGCCTTC AAC[989]	GTTTAGTTGTGTTTCATTT TCGTT [991]	TCATTTACTTCATCTGCAT CCTCTT [1067]	AAGATTTGTGGCATATCC TGAGTTA [1069]	AATATCAGTAATTCCAGA ACCAAGAAGAT [993]	ACTTGAGAAATTGCTGTT TTAACAAGTAG [1071]	GGGATAGTGGTGTATGTC TTTTAGAAATA [1073]
15		NO]	Y.	TG		၅၀	၁	T	А	<u> </u>	- C5	. Z
20		Primer forward [SEQ ID NO]	CGAATGATGCAATCA GACGAAA [982]	TTGAATCACCAAATTG AGGTTGT[984]	AAATCCATCGAGATG GTAATATATATCA [986]	GTATGCAATTTGATCG TGGTTAT [988]	ATGTATGŤTAĠĆACTC TTTAATGTTAAGTG [990]	CATCATTAATTCGATT CCCTGAAT [1066]	TCAATTTGACTTAAAA GAAGTTGGC [1068]	TGTCATATTATCAACA TGTAATCGAACTG [992]	TTGATAGACATAGAA GATTGAGATCATCAG [1070]	GTAAATTAGTCGTTG GCTCCAGAAG [1072]
25		Prir	CG GA	TT. AG	AAAT( GTAA' [986]	GT TG	ATGT, TTTA/ [990]	CA1 CC(	TC/ GA/	TGTC/ TGTA/ [992]	GA GA [10	GT/ GC
30	(continued)	gene probe SEQ ID NO	18	19	20	21	22	09	61	23	62	63
35			the fem									
40		suc	ssor; belongs to	ınit A	unit B	, protein	; protein			ctase		Φ
45		Functions	tase repres	ase IV subi	in beta sub	heat shock	heat shock	unit A	unit B	r RNA redu	e synthase	e deaminas
50			glutamine synthetase repressor; belongs to the fem C locus	DNA topoisomerase IV subunit A	gyrase-like protein beta subunit B	stress response; heat shock protein	stress response; heat shock protein	DNA gyrase subunit A	DNA gyrase subunit B	Glutamyl-transfer RNA reductase	Porphobilinogene synthase	Porphobilinogene deaminase
55		Gene symbol	glnR	grlA	grlB	groEL	groES	gyrA	gyrB	hemA	hеmВ	hemC

5	Primer reverse [SEQ ID NO]	AATGCATCGATTTGTTGA TGTTCTA [1075]	AATCCTCGACATTTAATG CACCTAC [995]	GTGGATATGGATCATTAT TCTTTTCG [997]	CTAATCTTAAAGTATCCAA TGTAGCTTCTGTA [999]	TGATATTCGTATAACGCA CACCATC [1077]	CTCTACGTACAATCGATA CTAATTCATTATCT [1001]	CTATAACCAAAACCTAAT GCTTGTGAC [1003]	GGCTAATGACACCTAAAG AGTTAACAACT [1005]	AATGTTTAACAAGCACTT CACGCT [1007]
15 20 25	Primer forward [SEQ ID NO]	TGTTGATAACATTGCT GTGATAGGAA [1074]	AAAATGATCAAAGGT GAAGAAACATC [994]	AATGGGATTATTAGTT ATGGCTTATGG [996]	ATGAGATATACGAAAT CAGAAGAAGCA [998]	ACAGAATCAACCTGT AGATGAGTACTTAGA T [1076]	AAACAGCAAGATCCT AATATTGATGTAAC [1000]	ATTAACAAAATTGATT TACCTGCTGC [1002]	AAAGACGCATCAAAA CCAGCA [1004]	GATTAACCACTTAGCA CTAAACACACCT [1006]
30 thou	gene probe SEQ ID NO	64	24	25	26	65	27	28	29	30
<i>35 40</i>	ons	ıase	oxylase			oorphyrinogen oxidase	tep of protoheme IX			
<i>45 50</i>	Functions	Uroporphyrinogene III synthase	Uroporphyrinogene decarboxylase	Ferrochelatase	GSA-1-Aminotransferase	oxygen-independent coproporphyrinogen oxidase	putative involved in a late step of synthesis	GTP-binding protein	holin-like protein LrgA	holin-like protein LrgA
55	Gene symbol	hemD	hemE	hemH	hemL	hemN	hemY	ІерА	IrgA	IrgB

5	Primer reverse [SEQ ID NO]	TGGCTGTTATACGCTTGG TTGT [1009]	ACATTTAGTACATTACCG CCACCTAC [1011]	TTAATTTAATTCTGGTCG GCTTTGT [1085]	TTAGCTGTATACTCGAAA TCCAATCC [1013]	TATTTCAGCAATGTCACC CGTATTA [1015]	TCACTATCTGGATCAGAA TCTTTAACAAT [1017]	AAGTGTGGTTGAAATA CTGCAA [1087]	ACACAGAGAATAACCAGG AGAAGA [1023]	TCAAGTTGCGAAATTAGC TGA [1025]
20 25	Primer forward [SEQ ID NO]	CGACAACACCCAAC AAGCA [1008]	GTTATCGTATTAACTG GTGAAGGTGATT [1010]	TTTAAGTCACAAATTG TAACACCGAA [1084]	CGTAAGGGAAGTAGT TATCAGTCCG [1012]	ATGGACTTTTGGTTAT ATAAACAAGCAC [1014]	ATTGATAATTTACATC CAACACCTGC [1016]	CTTGGGGTGATGATG AACATCTA [1086]	TCGTTTACATCATAAT AATCATCAGAC L10221	TIGTAATTCACTTAAC TTCACCAATG [1024]
30 (continued)	gene probe SEQ ID NO	31	32	69	33	34	35	70	38	39
40	Functions			ynthetase	t-cyclohexadiene-1-	CoA ligase		L-alanine synthetase	otein	otein
<i>45 50</i>	Fun	peptidoglycan hydrolase	naphthoate synthase	o-succinylbenzoic acid synthetase	2-Succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylase	O-succinylbenzoic acid-CoA ligas	Isochorismate-Synthase	UDP-N-acetylmuramoyl-L-alanine	DNA mismatch repair protein	DNA mismatch repair protein
55	Gene symbol	lytM	menB	menC	menD	menE	menF	murC	mutL	mutS

5		Primer reverse [SEQ ID NO]	TTGACACCATAACTCATTA TAGGAATATTG [1029]	TTGGTAACCAAACATTTTC AGCTT [1033]	TTGCTTTTACAGTTCTGTT TTCATCTAC [1035]	AGTGGTAAACCTGGAACG ATATCA [1091]	TTTCTACTGGCTCGTCTAT AACGC [1093]	GTAATTGTGAGT GTCCAT AAGAATCCA [1037]	ACGATCTGACACACCTAA AATGTA [1039]	CCCACATTGTTATTTTGTT TGTAT [1041]	CCTTTATCAATCGCAATG TC [1225]	AACTGAAGATAAGCCGTT TG [1227]
15	_	[]	<u> </u>		<u> </u>		. ,				O L	
20 25		Primer forward [SEQ ID NO]	GGTGTTCCAAACTCA AAAGATGATATA [1028]	TGACATTTCAAATCAA TCACATCG [1032]	CTGGAGATACTATTG AAGAAGACGATG [1034]	CAGGTAAATTAGTTGT AGTTGGTGGAG [1090]	ATTGTTACGTGCATTA GGTTTCTCA [1092]	TAGTTATCGAGATTAT CAAAGATTGGTAGA [1036]	TGAATCTTAATATAGA AACAACCACTCAAG [1038]	TCTAAAGAAGATTTTA TCGAAATG [1040]	GAAAGTATTCTGTAG GTACTGCTTC [1224]	CGGGCAAATAAATAA AGATG [1226]
30	(continued)	gene probe SEQ ID NO	14	43	44	72	73	45	46	47	139	140
35				1beta				JC	)r	)r	ly .	ý
40		SI		pyruvate dehydrogenase (lipoamlde): subunit E1beta	erase: subunit E2	ase: subunit E3		rnate sigma factor	rnate sigma factor	rnate sigma factor	serine-aspartate repeat protein multigene family	serine-aspartate repeat protein multigene family
45		Functions	synthase	ogenase (lipo:	e acetyltransf	e dehydrogen	B-subunit	encoding alte	encoding alte	encoding alte	repeat protei	repeat protei
50			porphobilinogen synthase	pyruvate dehydr	dihydrolipoamide acetyltransferas	dihydrolipoamide dehydrogenase: subunit E3	RNA polymerase B-subunit	putative operon encoding alternat	putative operon encoding alternat	putative operon encoding alternat	serine-aspartate	serine-aspartate
55		Gene symbol	<i>bqd</i>	pdhB	pdhC	Дирд	ров	rsbU	ısbV	rsbW	sdrC	sdrD

	Γ										
5		[SEQ ID NO]	ATGATGCA	SAATCTCT FATA	зтGАТАСА	.TCGGTCT 045]	ATGAATG 47]	GTAAAAGT	AATCGCTG	застсете	AACACAT ]
10		Primer reverse [SEQ ID NO]	GCAAAACAAGATGATGCA ACG [1229]	GAAATAGGTACAATCTCT GTAAAGTCCATATA [1043]	CTCTGAAGTCGTGATACA TGCA [1103]	ATATTAGCAAATCGGTCT TATCTCTCA [1045]	CTCCCAGAATAATGAATG GTTTAAAT [1047]	GGGATAGCACGTAAAAGT GGAA [1049]	GATTAATGACAATCGCTG GTGTG [1129]	CTTTGAACAGCACTCGTG CG [1051]	TCGTAGCTTCAAACACAT TTTCAA [1053]
15		<u></u>			<						
20		Primer forward [SEQ ID NO]	TCTGTCGCAGTTTTAT CAGTTGAAG [1228]	TGAGATAGATGCAAT CATGTTTATGG [1042]	GATGGTTCAACTGTTA CGCTATTA [1102]	AATATAATTGGGAAG AAGTACATCAAGAAG [1044]	TTGAATTACCAAAATT ACCATACG [1046]	GCGCATTTTGAAAAG GCA [1048]	CTGGTCCTGGATATA CTGGTTCTTT [1128]	TTCGTTGTTCATAGGT GCGAGT [1050]	TATTGCCTTATTTAGA TGTATTGCTTTT [1052]
25		Prim	TCT	TGAGA CATGT [1042]	GAT	AA AA( _[10	TTG	909 909	CT(	TTC	TATTG TGTAT [1052]
30	(continued)	gene probe SEQ ID NO	141	48	78	49	50	51	91	52	53
35									eins		
40		Suc	ein multigene family			repressor			tanspeptidase;sorta se that anchors surface proteins to the cell wall		
45		Functions	te repeat prot			al dependent	mutase	mutase	sorta se that a	proteins	protein
50			serine-aspartate repeat protein mult	G protein	sigma factor B	sit operon metal dependent repressor	superoxide dismutase	superoxide dismutase	tanspeptidase; to the cell wall	iron transport proteins	iron transport protein
55		Gene symbol	sdrE	dbs	sigB	sirR	sodA	<i>Bpos</i>	srtA	sstA	sstB

5	Primer reverse [SEQ ID NO]	TATTCAGTATCTTGTGCTA TTGTCATTG [1055]	AATTTTCGCTTTAGGTGC AGCT [1057]	CTCGAAATTAAGAAAGTA ACACC [1131]	AACGAAATACTGTTACT GGACCTAAAA [1109]	CAGCTAAGTTTTCTTTTG GTTGGA [1059]	GCTGTCGAATCATTTCTA AAATATACGT [1111]	AACCAATGATČTAGĪGTA AATGTTAAACCT [1061]		TTGATTCACTAATTCCTCC GCAT [953]	TTTAGCATCAGCAGCATT TACTACC [955]
15 20 25	Primer forward [SEQ ID NO]	AATCAAATGATATTGG AAGATATTAGCA [1054]	CATGCGGTAACAATT CTGATAAAGA [1056]	TTAACAATAGAACATT TAACAAAGAAG [1130]	GCATTTGGTACTAAA GATCCAGTCTACT [1108]	GCTGACTATGAAGGT AAAGCTGACA [1058]	ATTCATTTAGTCAGTG GTCATCCAAT [1110]	CAATTGGCTTTCGATT ATTGTTGTA [1060]		GCTTCAGTGCTTGTA GGTACGTTAA [952]	TAATGATACATCTGAT ATTAGTGCAAACAC [954]
30 :	(continued)	54	55	55	81	56	82	57		3	4
35 40					ase						
45 50	Functions	iron transport protein	iron transport protein	Potential ABC transporter	DNA-3-methyladenine glycosidase	thioredoxin reductase	prephenate dehydrogenase	yhiN-protein	Virulence Factors	clumping factor A	clumping factor B
55	Gene symbol	+	iron iron t	stpC Pote	tag DNA	<i>trx</i> thion	tyrA prep	<i>yhiN</i> .	Virul	clfA clum	clfB clum

	Γ											
5		Primer reverse [SEQ ID NO]	ATCAGGTTTAGTTGGTGG TG [1117]	GATTTTGTTTCAGATTCAC CGTATTT [957]	GCATTATTAGAGGCATGT GG [1119]	TTTCTAACTAGATTTTCAT CATACTGGC [1173]	TGGATAGCCTATTAATTC GAGTTTG [1175]	CAAAATATTGAGAATCAT TGAACATTTC [1177]	GCCAAAATAGTGCTTCAA TATCAGA [1123]	AGCGAAGGATACGGTCC AAG [1125]	AAACTGCACAACCAGCAA ATATAGA [1133]	GCGAGTTGATTTGCCATC GG [1127]
		Prim	ATCAGGT TG [1117]	GATTTTG CGTATTT [957]	GCATTATT GG [1119]	TTTCT	TGGA1 GAGTT	CAAAA TGAAC	GCCA/ TATCA	AGCGAAGGA AAG [1125]	AAACT ATATA	GCGAGTT GG [1127]
15	•	ID NO]	SAA	ıca	SAA	AAG	CCA '4]	ACA	rGA 22]	CAC	cgt ]	сттс
20		Primer forward [SEQ ID NO]	TCGAGGAATTAACAA AGGTC [1116]	TGTTAGGGATACACA ACATAAAACTGA [956]	GÄÄCCTAGCCATCAA GACAG [1118]	TATCTTTAGCATTAAG CGTTTATTCAAT [1172]	TGCATTTAATTTACCA AAAGAGCTT [1174]	AAGAGCTTTATACACA CATTACGGATAA [1176]	CTCTTTTTACCTTTGA CGTTGGATT [1122]	GCTTTTCTGTGTGCAC TGACAGT [1124]	TTACATCTGTACCCGT TTCCACTT [1132]	CCGCCTTAATTCCTTC TCCAAA [1126]
25	-		TCC	TGTT/ ACAT/ [956]	Gàv	TATCTI CGTTT/ [1172]	TGC	AAGAG CATTA( [1176]	CTC CG1	GCT	TTA TTC	000
30	(continued)	gene probe SEQ ID NO	85	5	98	113	114	115	88	68	93	06
35	-	-			~			·		~	<u> </u>	
40		9			itein	hibitor						
45		Functions	u.	ase	stin binding pro	differentiation ir	e A precursor	e B precursor	ng protein	ng protein	ing protein	ing protein
50			collagen adhesin	staphylocoagulase	cell surface elastin binding protein	Epidermal cell differentiation inhibito	exfoliative toxine A precursor	exfoliative toxine B precursor	fibrinogen binding protein	fibrinogen binding protein	fibronectin-binding protein	fibronectin-binding protein
55		Gene symbol	cna	coa	Sdqə	EDIN	eta	etb	<i>fbpA</i>	fib	fnbA	fnbB

5		Primer reverse [SEQ ID NO]	AGGTGCAGTTTTATCATT AGACGG [1065]	ATTTGAGCTACTTCATTAT CAGGTAGTTG [1187]	CTTTGATTGGGTAATGAT CTGAAAA [1189]	TAGTGAATTTGTTCACTG TGTCGATAA [1167]	GTGTTTTCCAGTTCACTTC ATATTTAACT [1181]	ATGTTTTGAGTTATAGCT AATCGTT [1179]	ATTTCACTTTGTGATTTTC CCAATC [1183]	CCAATTGACTTCATATTTC ACAGTGTA [1185]	GTGAAAGATGCCCTTGAG TGG [1169]	TATATCTCGAAGTTGCTA GTTGGGG [1171]
10		Primer reve	AGGTGCAGTTTT AGACGG [1065]	ATTTGAGCTACTTCAT CAGGTAGTTG [1187]	CTTTGATTGGGT/ CTGAAAA [1189]	TAGTGAATTTGTTC/ TGTCGATAA [1167]	GTGTTTTCCAGTTCA ATATTTAACT [1181]	ATGTTTTGAGTT/ AATCGTT [1179]	ATTTCACTTTG1 CCAATC [1183]	CCAATTGACTTCA1 ACAGTGTA [1185]	GTGAAAGA TGG [1169]	TATATCTCGAAGI GTTGGGG [1171]
15		NO]	CG	٨	CT _	<b>5</b>	T T	Ч	AC	AG t]	_	TT:
20		Primer forward [SEQ ID NO]	GAACAAGGGAATGCG ATAACG [1064]	ATGATGAAAATGAAA ACACGTATAGTC [1186]	TGTTAATAAAGGCACT CCAGAGTTC [1188]	TTTTATCTTAATTAAG GAAGGAGTGATTTC [1166]	ACTGAAGTAGAAAGT CAGAACTCTAAAGGT [1180]	CTTAAAATTAAATAGA AAGAAAGT [1178]	ATAGCTTCCACCCAAC ATATGGTAA [1182]	AATCAGCATTTGATAG CGATTTATTT [1184]	AAACATCAAATCGCT GTGGCT [1168]	GGGTTCTTGCTGTCTT TAAGTGATT [1170]
25		Prin	GA AT,	ATGATO ACACG [1186]	157 200	TTTTAT GAAGG [1166]	ACTGA CAGAA [1180]	CTT	ATA ATA	AA CG,	AAA GTC	GG(
30	(continued)	gene probe SEQ ID NO	59	120	121	110	117	116	118	119	<del>-</del>	112
35												
40		ns	er hydrolase				nt A; C-terminus	nt A; N-terminus	nt B	nt C; C-terminus		
45		Functions	r; glycerol est	c			sin componer	sin componer	sin componer	sin componer	e S	ein
50			lipase precursor; glycerol ester hydrolase	alpha-hemolysin	beta-hemolysin	delta-hemolysin	gamma-hemolysin component A; C-i	gamma-hemolysin component A; N-	gamma-hemolysin component B	gamma-hemolysin component C; C-	hyaluronate lyase	lgGbinding protein
55		Gene symbol	geh	hla	din	plq	hlgA_C	hlgA_N	higB	hlgC_C	hysA	lgGbg

5		Primer reverse [SEQ ID NO]	GATTGTTATTAGCGTTTG AATCTTGAC [1083]	GATGTATGAGTTGCTCTT ATGTGATCTTTA [1191]	GATCCTTCTAAATAACTAT TGCCATAGTG [1195]	AATCAAAGCATCTTTGTT₽ TACTTT [1193]	TGCATTTACCCAACCAGT GC [1197]	TTTCGCTTGTGCTTCACT	GCGCAAAGATCGAAGTCA CTTAT [1199]	TGCATGTTTTCAGAGTTA ATCGTTT [1201]	AGTTAGGTAATCTAATTCT TGAGCAGTCA [1203]	ATTCCTAGCTTTTATGTCT AGTTCTTGAG [1205]
15		[0]									<b>(</b> 5	
20 25		Primer forward [SEQ ID NO]	TTTTAAGTGGTGGAC AAGCACAA [1082]	CATATGGCAGAGATA GTTATCATTCAACT [1190]	AGTGTTCAATGGGGA ATAAAAGCTA [1194]	AACATTGTCGTTAGG AATAATCACT [1192]	ACTCAAACAGTTAGC AAGATTGCTC [1196]	GCGATTGATGGTGAT ACGGTT [1088]	CGAGTTATTTTGAACC AACAGGC [1198]	CTGATGTTTTTGATGG GAAGGTT [1200]	ATATATTCTATTAAGG ACACTAAGTTAGGGA AT [1202]	GGCACATGATTTAATT TATAACATTAGTG [1204]
30	(continued)	gene probe SEQ ID NO	89	122	124	123	125	71	126	127	128	129
35												
40		ns	os S				totoxin			precursor	precursor	precursor
45		Functions	er hydrola		minus	minus	nidase; cy			erotoxin A	erotoxin B	erotoxin C
50			lipase; glycerol ester hydrolase	leucocidin F	leucocidin S; C-terminus	leucocidin S; C-terminus	N-acetylglucosaminidase; cytotoxin	nuclease	staphylokinase	staphylococcal enterotoxin A precursor	staphylococcal enterotoxin B precursor	staphylococcal enterotoxin C precursor
55		Gene symbol	dil	lukF	lukS_C	lukS_N	NAG	unc	sak	sea	seb	sec

5		Primer reverse [SEQ ID NO]	TTTGACTT	GGTTTAAC 221]	ATAGTTTT [1223]		GCATAACC (3]	GATGCAGA	CAATCCAC	'GTCTCGCA	SAGATGGC	CCATTTGC	TCTGTTAC 741]
10		Primer revers	AGGTTAGCACTTTGACTT GG [1135]	CATTGTTGCTGGTTTAAC TACTTCAC [1221]	TTTCTGCTTCTATAGTTTT TATTTCATCA [1223]		CTTTTCTTTTGCATAACC TTTTTTC [2633]	CAGATGCGATGATGCAGA CC [2621]	CCAGTTTTCGCAATCCAC ATC [2637]	TCATTTAAAATGTCTCGCA ATTCTT [2575]	GCATTTTTCCCAGATGGC TT [2527]	TGCTTAATTTTCCATTTGC GAT [2601]	CATTTTTATCTTCTGTTAC CACTGGTT [2741]
15		[0]	<b>*</b>	(5	Ą.		<b>0</b> ⊢	ပ	<b>—</b>		F	() —	4
20		Primer forward [SEQ ID NO]	GGTATTGCATCTGTAA CTTTAGG [1134]	ACAAACGCAGTCAAG CAAACA [1220]	AAAATTACCTACTCCA ATAGAACTACCTTT [1222]		CCCTCATAAAATAA C	AAGCAGAGTTCAGCC ATGAATG [2620]	CTGGTGGGAGAAAT GAAAACC [2636]	AGCAAGTTGAAATAT CTATGGCTGA [2574]	GAAAATTCACGTATGT CATGGAATC [2526]	GATAAGAGATTTGCC TATGCTTCAA [2600]	TTGGATAGTTCAACAA AAACATTAACA [2740]
25		Prim	GG <sup>-</sup> CTT	ACA	AAAAT ATAGA [1222]		000' A00'	AAG	CTC GA/	AGC	GAA	GAT	TTGGA AAACA [2740]
30	(continued)	gene probe SEQ ID NO	94	137	138		843	837	845	814	790	827	897
35	-								Ę.				E <sub>n</sub>
40		ns	rotein A precursor			ninants	modifying enzyme	aminoglycoside acetyl transferase; kanamycin resistance	3' 5'-aminoglycoside acetyltransferase; kanamycin resistance				ing ATPase (Cadmium
45		Functions	G binding p	se gene	rom toxin	ance Detern	oglycoside	acetyl transf	side acetyltı		epressor		ım-transpor
50			immunoglobulin G binding protein A	V8 serine protease gene	toxic shock syndrom toxin	Antibiotic Resistance Determinants	bifunctional aminoglycoside modifyir	aminoglycoside a resistance	3' 5'-aminoglycos resistance	regulator protein	beta lactamase repressor	beta-lactamase	Probable cadmium-transporting ATF efflux ATPase)
55		Gene symbol	spa	sprV8	tst		aacA-aphD	aadD	aphA3	blal	blaR	blaZ	cadA

5	Primer reverse [SEQ ID NO]	acaaagatatgtgtgaa gttacc [2763]	GAAGCATGGTAACCATCA CATACA [2671]	AACATGACCAGATAACTC TTTAATTTCAT [2665]	AAAGAAATTGTTCCTTCG ATAGTTTATT [2651]	CGCTTGTAGAATCCTTCT TCAACA [2649]	TTGCATAATTTATGGTCTA TTTCAATG [2639]	AAAGGCACTAACACACGG TCTTT [2549]	TAAGTCACCAAATAAGAA TGGCG [979]	TGCACCATCTTGTTCAATT TGTT [2597]
<ul><li>15</li><li>20</li><li>25</li></ul>	Primer forward [SEQ ID NO]	TAGCAACCTCCCTTTC ATAC [2762]	CCTTCTTTGATTTATG CAATTATGG [2670]	ATGACATTATCAATAA TTGTCGCTCA [2664]	TAGCTATCTTATCGTT GAGAAGGGAT [2650]	AACCGATACCGTTTAC GAAATTG [2648]	AACACAGTCAAAACTT TATTACTTCAAAAC [2638]	TAGGATTTGAACATAC TGGATTCCA [2548]	TCAGGTGAAATGTTA GAATCAGCA [978]	GTTAACGATTGATGA AACGCAAA [2596]
30 (continued)	gene probe SEQ ID NO	808	862	859	852	851	846	801	16	825
35 40	ions	sessory protein homolog	sferase	; trimethoprim resistance				lin resistance	methicillin resistance	tureus FemA and FemB
45	Functions	Cadmium efflux system accessor	chloramphenicol acetyltransferase	S1 dihydrofolate reductase; trimethoprim resistance	rRNA methylase	adenine methylase	adenine methylase	factor essential for methicillin resistance	putative factor essential for methicillin resistance	similar to Staphylococcus aureus proteins
55	Gene symbol	cadC	cat	dfrA	ermA	ermB	ermC	femA	fem D	fmhA

5	Primer reverse [SEQ ID NO]	TTCAGGATGTTCCTTTTCT AAAGCT [2583]	GGTCTTTTCTGTTAATTC ATAACCG [2647]	CTAATAGATGTGAAGTCG CTTTTCCT [2551]	TTTCATCTTGTGATAGATC TTCTTTTTC [2571]	TCGCCTTTTAAATGTGTA GCAAA [2543]	GACAAACGTACAGGATG TCCATAA [2761]	ATCAGCTAATGAAATGAA GATTGCA [1019]	GCAAGACTCACATACACC ATAAACTTC [1021]	CTTTTAGATGAACCTACA AATCACTTGG [2655]
20 25	Primer forward ISEQ ID NOI	GAGTTATTAAATAGTT TTGAACGCCG [2582]	GATATAGGATACAAA ATAGAAGTTGATTGG [2646]	ATATGAGATAGGCAT CGTTCCAAA [2550]	TAATAAAACGTATGAA ATATCATCTGCA [2570]	TTTAAAGAATGGAAC CAAGATCAAA [2542]	GCAGTATTAGTACTTG ATGAACCAACG [2760]	ATGAGGTACTCTTTAA TTAGTGGTATCTTGA [1018]	GAAAATACAGAACTT GATGGTGAAATG [1020]	TCATAAGCTGACAGA TTTTCGATCC [2654]
30	(continued) gene probe SEQ ID NO	818	850	802	812	798	206	36	37	854
40	Functions	glycine 1 to peptidoglycan	lyltransferase	22,						ductase
45 50		essential for addition precursor	lincosaminide nucleotidyltransferase	penicillin binding protein 2'	med protein	med protein	ABC transporter	ABC transporter	ABC transporter	methionine sulfoxide reductase
55	Gene symbol	fmhB	linA	mecA	mecl	mecR	mreA	тгеВ	mreR	msrA

5	Primer reverse [SEQ ID NO]	ACAGTGTTTCAAATGCCG ATAAA [2755]	CTATCCCAATCCATAGAC GTGTTAA [1031]	GCCCACTACAGATTCTTC AGCTAC [2717]	AAAGAGGTATAGCCCATT CTGCA [2635]
15	[ON 0	ī	۸T آ	ГТ	ГТ 34]
20	Primer forward [SEQ ID NO]	TTAGCTTTCATAATGT CAGTTGTATTGA [2754]	AACACAATCGGAAAT GTTGGATAC [1030]	CAATGGTTACAGGTT GTGGAAGA [2716]	ATATCAGGAAAGATT GGAAATACGG [2634]
30 (continued)	gene probe SEQ ID NO	904	42	885	844
35					
40	SL		2b	ound resistance protein	
45	Functions	quinolone resistance protein	penicillin-binding protein Pbp2b	quaternary ammonium compound	adenyltransferase AAD9
50		quinolone	oenicillin-b	quaternary	adenyltran
55	Gene symbol	norA	д <i>Нар</i> е	gacA q	e ods

[0126] In order to obtain a high specificity level, each selected gene was compared to all other gene sequences available in the NCBI database using the BLAST algorithm. From that comparison, regions (ranging from 104 to 1434 bp) devoid of apparent homology with genes of other bacterial species and *Homo sapiens* were defined and amplified by PCR using specifically designed primers (see Tab. 6). A mixture of the total DNA from three different *S. aureus* reference strains and 100 clinical isolates was used as template for amplification of *S. aureus* gene segments, increasing therefore the chances to amplify more seldom occurring virulence and antibiotic resistance genes. PCR products were cloned into the plasm id pCR 2.1 -Topo Vector (Invitrogen, Karlruhe, Germany) which were used to transform competent *Escherichia coli* (XL-1-Blue) cells using the Calcium Chloride protocol (Seidman, C.E. et al., in: Ausubel, F.M. (ed.), Current Protocols in Molecular Biology, John Wiley & Sons, Inc. (2000)). Recombinant plasmids containing selected gene segments were screened by restriction analysis and verified by sequencing. The plasmid library constructed was used for re-amplification and production of the bulk DNA (10 μg at a concentration of 1 μM) from each clone necessary for printing the microchips. A Microgrid II spotter (BioRobotics, Cambridge, UK) and CMT-GAPS<sup>™</sup> coated glass slides (Corning Incorporated, Corning, USA) were used. The complete array of 140 segments of genes was spotted in 3 replicates per slide.

#### C) DNA purification

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#### a) Sample preparation

[0127] <u>Bacterial cultures:</u> Overnight cultures (5 ml) were harvested at 2,560g for 10 minutes. After discarding the supernatant the pellet was washed in 1 ml TE (10 mM Tris-HCl, pH 7.5 - 1 mM EDTA) and recovered by centrifugation at 17,900 g for 2 min.

[0128] <u>Blood cultures:</u> One ml of blood culture was mixed with 1 ml 0.1% Triton®-X-100 and kept at room temperature for 5 min in order to disrupt blood human cells and resolve bacterial clumps. Bacterial cells were then harvested at 17,900 g for 10 min. Pellets were washed in 1 ml TE and recovered as described above.

#### b) Purification of DNA

[0129] Pellets of harvested cells were resuspended in 500 μl lysis buffer (20 m M Tris-HCl, pH 8.0 - 2 mM EDTA, pH 8.0 - 1.2% Triton®-X-100). To promote bacterial lysis, lysozyme and lysostaphin (Sigma, Taufkirchen, Germany) were added to reach a final concentration of 0.8 mg/ml and 0.2 mg/ml respectively. To lyse Gram negative bacterial cells, only lysozyme in the indicated concentration was used. Samples were then incubated for one hour at 37°C. After treatment with Proteinase K (1 mg/ml) (Sigma, Taufkirchen, Germany) for 5 hours at 55 °C under mild agitation, the samples were heated at 65°C for 30 min to inactivate Proteinase K and then cooled down to 37°C. Finally, a RNAse A treatment (0.2 mg/ml) was carried out for 1 hour at 37°C. A pretreatment with CTAB (Cethyltrimethylammonium bromide) was performed in order to release DNA from polysaccharide DNA complexes (Murray, M.G. and Thopson, W.F., Nucl. Acid Res. 8: 4321-4325 (1980)). Salt concentration was adjusted to 0.7 M by adding 5 M NaCl. After thoroughly mixing, a 10% CTAB-0.7M NaCl solution was added to adjust the CTAB concentration to 1%.

[0130] The mixture was subsequently incubated under rotation for 20 min at 65 °C and then extracted with one volume of chloroform/isoamyl alcohol (24:1). The samples were spun in a microcentrifuge (17,900 g) at room temperature. The aqueous phase was extracted once with chloroform/isoamyl alcohol (24:1), once with phenol/chloroform/isoamyl alcohol (25:24:1) and finally with chloroform/ isoamyl alcohol (25:24:1). Genomic DNA in the aqueous phase was sonified (3 x 10 s at 12% amplitude with 20 s breaks between pulses) in a Digital Sonifier (Branson, Schwaebisch Gmuend, Germany) to obtain fragments of around 1 kb, then precipitated with one volume of isopropanol and pelleted by centrifugation for 30 min at 4°C in a microcentrifuge at 17,900 g. The pellets were washed in 70% ethanol and resuspended in 50-100  $\mu$ l TE (10 mM Tris-HCl, pH 7.5 - 1 m M EDTA). This DNA preparation was used when a high yield (hundreds of  $\mu$ g) was necessary, for example to prepare samples for several hybridisations experiments.

[0131] A second protocol using DNeasy Tissue Kit (QIAGEN, Hilden, Germany) adapted to bacterial cells and allowing DNA preparation in two hours, was also used when fast preparation was the priority. The abbreviations below pertain to the manufacturer's abbreviations for buffers used in the kit. The bacterial pellet was resuspended in 1 ml ddH $_2$ O and the cell suspension frozen in liquid N $_2$  for 1 minute and then placed in a 60°C thermo-block for 2 minutes. Such a treatment was repeated once and bacteria were centrifuged again for 5 minutes at 14,000g. The resulting pellet was resuspended in 180  $\mu$ l lysis buffer (20 mM Tris-HCl, pH 8.0 - 2 mM EDTA, pH 8.0 - 1.2% Triton-X-100). Specifically for *S. aureus* DNA preparation, lysostaphin (0.2mg/ml) was added and incubated 1 hour at 37°C. After, 200  $\mu$ l of buffer AL (for gram positive bacteria) or buffer ATL (for gram negative) and 25  $\mu$ l of the Proteinase K solution delivered with the kit were added and incubated at 70°C for 30 minutes. 200  $\mu$ l of 100% ethanol were added and the suspension transferred to a DNeasy Mini Column placed into a collection tube. The column was centrifuged at 6,000 g for 1 minute, washed first with 500  $\mu$ l of buffer AW1, centrifuged at 6,000 g for 1 minute, washed then with 500  $\mu$ l of buffer AW2, and centrifuged

at 14,000 g for 3 minutes. The column was then placed in a 1.5 ml tube and centrifuged once more at 14,000 g for 1 minute. DNA was eluted with 130  $\mu$ l of buffer AE. After one minute the column was centrifuged at 6,000g for 1 minute. The eluate was re-loaded in the column and centrifuged again under the same conditions in order to increase the DNA yield.

#### D) DNA labelling

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[0132] Different amounts of DNA (5 ng to 5  $\mu$ g) were labelled with 3  $\mu$ l either of Cy5-dCTP or Cy3-dCTP (Amersham Pharmacia Biotech Europe, Freiburg, Germany) by random priming (1 x random primer/Klenow reaction buffer) using Klenow Polymerase (50units) (both from BioPrime DNA labelling Kit, Invitrogen, Karlsruhe, Germany) in the presence of 0.12 mM dATP's, dGTP's and dTTP's and 0.06 mM dCTP's, in a total volume of 50  $\mu$ l. After 2 hours incubation at 37°C, the reaction was interrupted by adding 5  $\mu$ l of 0.5 M EDTA and the probe purified either by MiniElute PCR or QIAquick Purification Kits (QIAGEN, Hilden, Germany), depending on the amount of labelled DNA applying two wash and two elution steps.

#### E) Hybridisation and detection procedure

**[0133]** All experiments described in the present example represent co-hybridisation of two different DNA samples labelled respectively with Cy3 and Cy5. Cy3 and Cy5 belong to the cyanine family of fluorophores and were used as reporter molecules. The photochemical properties of the two CyDye fluors were as follows: Absorption maximum at 550 nm and emission maximum at 570 nm for Cy3 and for Cy5 at 649 nm and 670 nm, respectively.

**[0134]** After purification, Cy3 and Cy5 labelled DNA were pooled and 10  $\mu$ g of Salmon Sperm DNA and 50  $\mu$ g of polyA DNA were added. The mixture was frozen in liquid nitrogen and lyophilized in the dark. DNA microchips were automatically hybridised in a GeneTac Hybridisation Station (Genomic Solutions, Harvard, USA) following the Corning protocol.

[0135] Shortly, 110  $\mu$ l of pre-hybridisation buffer (25% Formamide, 5x SSC, 0.1% SDS, 10 mg/ml BSA) were added to each slide and incubated for one hour at 42°C. Lyophilized samples were resuspended in 110 $\mu$ l of hybridisation buffer (25% Formamide, 5x SSC, 0.1% SDS), denatured for 3 minutes at 90°C, added to the slides, and incubated 4 hours at 42°C. After several washing steps using successively 2 x SSC/0.1% SDS, 0.1 x SSC/0.1% SDS, and 0.1 x SSC, slides were dried by a 2 min centrifugation step (1000 g) and read in a Scan Array 5000 (Perkin Elmer, Boston, USA) using emission filters for Cy3 and Cy5 in two separate channels. Fluorescence intensities as hybridisation indicators were then analyzed by the software ImaGene (BioBiscovery, Marina Del Rey, USA). Spots were found and segmented in order to select areas of recognizable signals for analysis. Intensity of fluorescence of each spot was measured, signal to local background ratios were calculated, spot morphology and deviation from expected spot position were considered. Cut off values for those parameters were empirically determined in pilot experiments and used to tag spots either as positive or as negative.

#### F) Validation of the detection system

[0136] The experimental approach adopted in present example required dual-dye hybridisations. It was therefore necessary to verify at first whether DNA samples from the same source, labelled with one or the other fluorochrome, would produce the same hybridisation pattern. Co-hybridisation experiments, combining two identical samples of 2 μg of *S. aureus* DNA, produced strictly similar hybridisation results whatever fluorochrome was used for labelling (Fig. 2A). For better presentation gray scale images from scanning were converted in false-color, where green and red color represent intensity of Cy3 and Cy5 fluorochromes respectively. All spots showed double-hybridisation - yellow color meaning the overlay between green (here assigned to Cy3 labelled DNA) and red signals (Cy5 labelled DNA). Signal intensities from both channels strongly correlated (r²=0,97) (Fig. 2B).

#### G) Sensitivity of detection

[0137] S. aureus DNA samples in decreasing amounts (from 2  $\mu$ g to 5 ng) were labelled and hybridised in order to determine the minimum amount of DNA producing the expected hybridisation pattern for a certain strain. Such expected patterns were defined as those produced by the hybridisation of 2  $\mu$ g of DNA. From 2  $\mu$ g to 50 ng no significant differences in the hybridisation pattern were observed with no false negative spots. Detection of 20 ng DNA was still satisfying with only 5% of false negative and false positive. However, 5 ng of labelled DNA yielded weak signals with almost 95% of false negative spots (data not shown). The limit of sensitivity of the S. aureus microarray was then considered as being 20 ng DNA which corresponds approximately to 7 x 10<sup>6</sup> S. aureus CFU (S. aureus genome 2.5 x 10<sup>6</sup> bp. 2.8 fg DNA per cell).

#### H) Specificity of detection

**[0138]** The specificity of the *S. aureus* microchip was demonstrated by six independently performed co-hybridisation experiments. Visual examination of pictures showing results of co-hybridisation of *S. aureus* DNA with *Pseudomonas aeruginosa* or *Escherichia coli* DNA revealed no cross-hybridisation between *S. aureus* selected gene segments and DNA probes from those Gram negative bacteria (data not shown). Transcribing these data in a bar code showing positive or negative spots (Fig. 3A and B) confirmed that only the *S. aureus* DNA sample hybridised with spotted probes.

**[0139]** The specificity of the microarray could be demonstrated even below the genus level. As shown in Fig. 4, some spotted S. *aureus* probes cross-hybridised with *S. epidermidis* and *S. saprophyticus* DNA samples. This is not surprising as these species are phylogenetically closely related. However, genes coding for *S. aureus* specific proteins as nuclease (*nuc*), clumping factors A and B (*clfA* and *B*), protein A (*spa*), V8 serine protease (*sprV8*) and alpha and beta hemolysins (*hla* and *hlb*) exclusively hybridised with *S. aureus* DNA. The presence/absence of such genes allowed unambiguous discrimination between *S. aureus* and CoNS.

#### l) *S. aureus* strain profiling

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**[0140]** The principle of the *S. aureus* microarray was tested as a tool for strain profiling. A distinctive hybridisation pattern could be established for reference strains and 10 selected clinical isolates. For instance when DNA from clinical isolates T100 and T103 were labelled with Cy5 and Cy3, respectively, and co-hybridised, both isolates were identified as *S. aureus*, since both contained species-specific genes as e.g. clumping factor A and B (Fig. 5A).

**[0141]** Moreover, both strains are methicillin resistant (*mecA* positive), but only T100 contained the beta-lactamase gene. The hybridisation of T103 DNA reveals the presence of *ermA*, *ermB* and *aacA* genes indicating that the strain is resistant to erythromycin and aminoglycosides.

**[0142]** Apparently, T103 harbors the genes encoding enterotoxines A (*eta*) and B (*etb*) while in T100 the gene encoding enterotoxin C (*etc*) is present. The presence or absence of these genes was confirmed by PCR assays (Fig. 5B) and the antibiotic resistance was verified by classical antibiograms ( Sahm, D. & Washington, J. A. (1991). Antibacterial susceptibility tests: dilution methods. In: Manual of Clinical Microbiology (Balows, A., Ed.), pp. 1105-16. American Society for Microbiology, Washington DC, USA) (data not shown).

#### J) Detection of S. aureus in spiked positive BACTEC® cultures

**[0143]** One possible application of the *S. aureus* microarray is to detect the bacterium growing in blood culture, i.e. after the BACTEC® signals bacterial growth. Blood culture bottles were spiked with 100 CFU of *S. aureus*. After the automated culturing system indicated bacterial growth, 1 ml was withdrawn for DNA extraction.

[0144] As shown in Fig. 6A, DNA samples prepared from sterile blood culture show no crosshybridisation with spotted S. *aureus* probes. A 2  $\mu$ g DNA sample derived from blood culture containing *S. aureus* cells revealed a hybridisation pattern almost completely identical to a DNA sample isolated from an overnight LB culture inoculated with a *S. aureus* colony (Fig. 6B).

**[0145]** These data underscore the high sensitivity and specificity of the detection system since blood culture DNA comprises a mixture of human and bacterial DNA. Co-hybridisation between DNA from blood culture positive for *S. aureus* and CoNS DNA also allowed clear identification since only the *S. aureus* probe hybridised to *S. aureus* species-specific genes (data not shown).

#### K) Detection of S. aureus in positive BACTEC® cultures inoculated with clinical specimens

**[0146]** Co-hybridisation with DNA from clinical blood cultures positive for *S.aureus* and CoNS (*Staphylococus epidermidis*), *Streptococcus mitis*, *E. coli* and *Klebsiella oxytoca* allowed clear species identification since the *S.aureus* probes hybridised to *S.aureus* species-specific genes only. *Staphylococcus epidermidis* positive blood culture DNA hybridised to staphylococcal metabolic genes and to some antibiotic resistance determinant genes only. No cross-hybridisation was detected between DNA from the two gram-negative strains and the *Streptococcus* strain and *S. aureus* spotted gene probes (data not shown).

Sequence Listing - Free text

55 **[0147]** a) Probe sequences

SEQ ID NO	Probe name	Template source
1	cataSaur_1_1	Staphylococcus aureus
2	cataSaur_1_2	Staphylococcus aureus
3	clfA_1_1	Staphylococcus aureus
4	clfB_1_1	Staphylococcus aureus
5	coa_1_1	Staphylococcus aureus
6	coa_1_2	Staphylococcus aureus
7	I-clpC_1_1	Staphylococcus aureus
8	I-clpP_1_1	Staphylococcus aureus
9	I-ctaA_1_1	Staphylococcus aureus
10	I-ctsR_1_1	Staphylococcus aureus
11	I-dltA_1_1	Staphylococcus aureus
12	I-dltB_1_1	Staphylococcus aureus
13	I-dltC_1_1	Staphylococcus aureus
14	I-dnaK_1_1	Staphylococcus aureus
15	I-elkT_1_1	Staphylococcus aureus
16	I-femD_1_1	Staphylococcus aureus
17	l-glnA_1_1	Staphylococcus aureus
18	I-glnR_1_1	Staphylococcus aureus
19	l-grlA_1_1	Staphylococcus aureus
20	I-grlB_1_1	Staphylococcus aureus
21	I-groEL_1_1	Staphylococcus aureus
22	I-groES_1_1	Staphylococcus aureus
23	I-hemA_1_1	Staphylococcus aureus
24	I-hemE_1_1	Staphylococcus aureus
25	I-hemH_1_1	Staphylococcus aureus
26	I-hemL_1_1	Staphylococcus aureus
27	I-hemY_1_1	Staphylococcus aureus
28	I-lepA_1_1	Staphylococcus aureus
29	I-lrgA_1_1	Staphylococcus aureus
30	I-lrgB_1_1	Staphylococcus aureus
31	I-lytM_1_1	Staphylococcus aureus
32	I-menB_1_1	Staphylococcus aureus
33	I-menD_1_1	Staphylococcus aureus
34	I-menE_1_1	Staphylococcus aureus
35	I-menF_1_1	Staphylococcus aureus
36	I-mreB_1_1	Staphylococcus aureus
37	I-mreR_1_1	Staphylococcus aureus
38	I-mutL_1_1	Staphylococcus aureus
39	I-mutS_1_1	Staphylococcus aureus

(continued)

SEQ ID NO	Probe name	Template source
40	I-NAG_1_1	Staphylococcus aureus
41	I-pbg_1_1	Staphylococcus aureus
42	I-pbpF_1_1	Staphylococcus aureus
43	I-pdhB_1_1	Staphylococcus aureus
44	I-pdhC_1_1	Staphylococcus aureus
45	I-rsbU_1_1	Staphylococcus aureus
46	I-rsbV_1_1	Staphylococcus aureus
47	I-rsbW_1_1	Staphylococcus aureus
48	I-sgp_1_1	Staphylococcus aureus
49	I-sirR_1_1	Staphylococcus aureus
50	I-sodA_1_1	Staphylococcus aureus
51	I-sodB_1_1	Staphylococcus aureus
52	I-sstA_1_1	Staphylococcus aureus
53	I-sstB_1_1	Staphylococcus aureus
54	I-sstC_1_1	Staphylococcus aureus
55	I-sstD_1_1	Staphylococcus aureus
56	I-trx_1_1	Staphylococcus aureus
57	I-yhiN_1_1	Staphylococcus aureus
58	epiP-bsaP_1_1	Staphylococcus aureus
59	geh_1_1	Staphylococcus aureus
60	gyrA_1_1	Staphylococcus aureus
61	gyrB_1_1	Staphylococcus aureus
62	hemB_1_1	Staphylococcus aureus
63	hemC_1_1	Staphylococcus aureus
64	hemD_1_1	Staphylococcus aureus
65	hemN_1_1	Staphylococcus aureus
66	hsdS_1_1	Staphylococcus aureus
67	hsdS_2_1	Staphylococcus aureus
68	lip_1_1	Staphylococcus aureus
69	menC_1_1	Staphylococcus aureus
70	murC_1_1	Staphylococcus aureus
71	nuc_1_1	Staphylococcus aureus
72	pdhD_1_1	Staphylococcus aureus
73	rpoB_1_1	Staphylococcus aureus
74	SAV0431_1_1	Staphylococcus aureus
75	SAV0439_1_1	Staphylococcus aureus
76	SAV0440_1_1	Staphylococcus aureus
77	SAV0441_1_1	Staphylococcus aureus

(continued)

SEQ ID NO	Probe name	Template source
78	sigB_1_1	Staphylococcus aureus
79	spa_1 _2	Staphylococcus aureus
80	sstC_1_1	Staphylococcus aureus
81	tag_1 _1	Staphylococcus aureus
82	tyrA_1_1	Staphylococcus aureus
83	I-aroC_1_1	Staphylococcus aureus
84	I-aroA_1_1	Staphylococcus aureus
85	I-cna_1_1	Staphylococcus aureus
86	I-ebpS_1_1	Staphylococcus aureus
87	I-eno_1_1	Staphylococcus aureus
88	I-fbpA_1_1	Staphylococcus aureus
89	I-fib_1_1	Staphylococcus aureus
90	I-fnbB_1_1	Staphylococcus aureus
91	I-srtA_1_1	Staphylococcus aureus
92	I-stpC_1_1	Staphylococcus aureus
93	I-fnbA_1_1	Staphylococcus aureus
94	I-spa_1_1	Staphylococcus aureus
95	I-aroE_1_1	Staphylococcus aureus
96	I-aroF_1_1	Staphylococcus aureus
97	I-aroG_1_1	Staphylococcus aureus
98	I-asp23_1_1	Staphylococcus aureus
99	I-atl_1_1	Staphylococcus aureus
100	bsaE_1_1	Staphylococcus aureus
101	bsaG_1_1	Staphylococcus aureus
102	cap5h_1_1	Staphylococcus aureus
103	cap5i_1_1	Staphylococcus aureus
104	cap5j_1_1	Staphylococcus aureus
105	cap5k_1_1	Staphylococcus aureus
106	cap8H_1_1	Staphylococcus aureus
107	cap81_1_1	Staphylococcus aureus
108	cap8J_1_1	Staphylococcus aureus
109	cap8K_1_1	Staphylococcus aureus
110	I-hld_1_1	Staphylococcus aureus
111	I-hysA_1_1	Staphylococcus aureus
112	I-lgGbg_1_1	Staphylococcus aureus
113	EDIN_1_1	Staphylococcus aureus
114	eta_1_1	Staphylococcus aureus
115	etb_1_1	Staphylococcus aureus

(continued)

SEQ ID NO	Probe name	Template source
116	hglA_1_1	Staphylococcus aureus
117	hglA_2_1	Staphylococcus aureus
118	hglB_1_1	Staphylococcus aureus
119	hglC_2_1	Staphylococcus aureus
120	hla_1_1	Staphylococcus aureus
121	hlb_1_2	Staphylococcus aureus
122	lukF_1_1	Staphylococcus aureus
123	lukS_1_1	Staphylococcus aureus
124	lukS_2_1	Staphylococcus aureus
125	NAG_1_1	Staphylococcus aureus
126	sak_1_1	Staphylococcus aureus
127	sea_1_1	Staphylococcus aureus
128	seb_1_1	Staphylococcus aureus
129	sec1_1_1	Staphylococcus aureus
130	seg_1_1	Staphylococcus aureus
131	seh_1_1	Staphylococcus aureus
132	sel_1_1	Staphylococcus aureus
133	set 15_1_1	Staphylococcus aureus
134	set6_1 _1	Staphylococcus aureus
135	set7_1_1	Staphylococcus aureus
136	set8_1 _1	Staphylococcus aureus
137	sprV8_1_1	Staphylococcus aureus
138	tst_1 _1	Staphylococcus aureus
139	I-sdrC_1_1	Staphylococcus aureus
140	I-sdrD_1_1	Staphylococcus aureus
141	I-sdrE_1_1	Staphylococcus aureus
142	b1169_1_1	Escherichia coli
143	envZ_1_1	Escherichia coli
144	fliCb_1_1	Escherichia coli
145	nfrB_1_1	Escherichia coli
146	nlpA_1_1	Escherichia coli
147	pilAe_1_1	Escherichia coli
148	yacH_1_1	Escherichia coli
149	yagX_1_1	Escherichia coli
150	ycdS_1_1	Escherichia coli
151	yciQ_1_1	Escherichia coli
152	ym cA_1_1	Escherichia coli
153	b1202_1_1	Escherichia coli

(continued)

SEQ ID NO	Probe name	Template source
154	eae_1_1	Escherichia coli
155	eltB_1_1	Escherichia coli
156	escR_1_1	Escherichia coli
157	escT_1_1	Escherichia coli
158	escU_1_1	Escherichia coli
159	espB_1_1	Escherichia coli
160	fes_1_1	Escherichia coli
161	fes_2_1	Escherichia coli
162	fteA_1_1	Escherichia coli
163	hlyA_1_1	Escherichia coli
164	hlyB_1_1	Escherichia coli
165	iucA_1_1	Escherichia coli
166	iucB_1_1	Escherichia coli
167	iucC_1_1	Escherichia coli
168	papG_1_1	Escherichia coli
169	rfbE_1_1	Escherichia coli
170	shuA_1_1	Escherichia coli
171	SLTII_1_1	Escherichia coli
172	toxA- LTPA_1_1	Escherichia coli
173	VT2vaB_1_1	Escherichia coli
174	ardeSE0106_1_1	Staphylococcus epidermidis
175	ardeSE0107_1_1	Staphylococcus epidermidis
176	aroiSE0105_1_1	Staphylococcus epidermidis
177	atlE_1_1	Staphylococcus epidermidis
178	agrB_1_1	Staphylococcus epidermidis
179	agrC_1_1	Staphylococcus epidermidis
180	alphSE1368_1_1	Staphylococcus epidermidis
181	gad_1_1	Staphylococcus epidermidis
182	glucSE1191_1_1	Staphylococcus epidermidis
183	hsp10_1_1	Staphylococcus epidermidis
184	icaA_1_1	Staphylococcus epidermidis
185	icaB_1_1	Staphylococcus epidermidis
186	mvaSSepid_1_1	Staphylococcus epidermidis
187	nitreSE1972_1_1	Staphylococcus epidermidis
188	nitreSE1974_1_1	Staphylococcus epidermidis
189	nitreSE1975_1_1	Staphylococcus epidermidis
190	oiamtSE1209_1_1	Staphylococcus epidermidis
191	ORF1Sepid_1_1	Staphylococcus epidermidis

(continued)

SEQ ID NO	Probe name	Template source
192	ORF3bSepid_1_1	Staphylococcus epidermidis
193	qacR_1_1	Staphylococcus epidermidis
194	sin_1_1	Staphylococcus epidermidis
195	ureSE1861_1_1	Staphylococcus epidermidis
196	ureSE1863_1_1	Staphylococcus epidermidis
197	ureSE1864_1_1	Staphylococcus epidermidis
198	ureSE1865_1_1	Staphylococcus epidermidis
199	ureSE1867_1_1	Staphylococcus epidermidis
200	gcaD_1_1	Staphylococcus epidermidis
201	hld_orf5_1_1	Staphylococcus epidermidis
202	icaC_1_1	Staphylococcus epidermidis
203	icaD_1_1	Staphylococcus epidermidis
204	icaR_1_1	Staphylococcus epidermidis
205	psm_betaiand2_1_1	Staphylococcus epidermidis
206	purR_1_1	Staphylococcus epidermidis
207	spoVG_1_1	Staphylococcus epidermidis
208	yabJ_1_1	Staphylococcus epidermidis
209	folQShaemolyt_1_1	Staphylococcus haemolyticus
210	mvaCShaemolyticus_1_1	Staphylococcus haemolyticus
211	mvaDShaemolyt_1_1	Staphylococcus haemolyticus
212	mvaK1Shaemolyticus_1_1	Staphylococcus haemolyticus
213	mvaSShaemolyticus_1_1	Staphylococcus haemolyticus
214	RNApolsigm_1_1	Staphylococcus haemolyticus
215	lipShaemolyt_1_1	Staphylococcus haemolyticus
216	agrB2Stalugd_1_1	Staphylococcus lugdunensis
217	agrC2Stalugd_1_1	Staphylococcus lugdunensis
218	agrCStalugd_1_1	Staphylococcus lugdunensis
219	slamStalugd_1_1	Staphylococcus lugdunensis
220	fblStalugd_1_1	Staphylococcus lugdunensis
221	slushABCStalugd_1_1	Staphylococcus lugdunensis
222	RNApolsigmSsapro_1_1	Staphylococcus saprophyticus
223	RNApolsigmSsapro_1_2	Staphylococcus saprophyticus
224	msrw1Stwar_1_1	Staphylococcus warneri
225	nukMStwar_1_1	Staphylococcus warneri
226	proDStwar_1_1	Staphylococcus warneri
227	proMStwar_1_1	Staphylococcus warneri
228	sigrpoStwar_1_1	Staphylococcus warneri
229	tnpStwar_1_1	Staphylococcus warneri

(continued)

230         gehAStwar_1_1         Staphylococcus warneri           231         ARG56_1_1         Candida albicans           232         ASL43f_1_1         Candida albicans           233         BGL2_1_1         Candida albicans           234         CACHS3_1_1         Candida albicans           235         CCT8_1_1         Candida albicans           236         CDC37_1_1         Candida albicans           237         CEF3_1_1         Candida albicans           238         CHS1_1_1         Candida albicans           239         CHS2_1_1         Candida albicans           240         CHS4_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         Striphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans	SE	EQ ID NO	Probe name	Template source
232         ASL431_1         Candida albicans           233         BGL2_1_1         Candida albicans           234         CACHS3_1_1         Candida albicans           235         CCT8_1_1         Candida albicans           236         CDC37_1_1         Candida albicans           237         CEF3_1_1         Candida albicans           238         CHS1_1_1         Candida albicans           239         CHS2_1_1         Candida albicans           240         CHS4_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251	23	30	gehAStwar_1_1	Staphylococcus warneri
233   BGL2_1_1   Candida albicans	23	31	ARG56_1_1	Candida albicans
CACHS3_1_1   Candida albicans	23	32	ASL43f_1_1	Candida albicans
235         CCT8_1_1         Candida albicans           236         CDC37_1_1         Candida albicans           237         CEF3_1_1         Candida albicans           238         CHS1_1_1         Candida albicans           239         CHS2_1_1         Candida albicans           240         CHS4_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255	23	33	BGL2_1_1	Candida albicans
236         CDC37_1_1         Candida albicans           237         CEF3_1_1         Candida albicans           238         CHS1_1_1         Candida albicans           239         CHS2_1_1         Candida albicans           240         CHS4_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256	23	34	CACHS3_1_1	Candida albicans
237         CEF3_1_1         Candida albicans           238         CHS1_1_1         Candida albicans           239         CHS2_1_1         Candida albicans           240         CHS4_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257	23	35	CCT8_1_1	Candida albicans
Candida albicans	23	36	CDC37_1_1	Candida albicans
239         CHS2_1_1         Candida albicans           240         CHS4_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1_1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257         GSC1_1_1         Candida albicans           258         GSL1_1_1         Candida albicans	23	37	CEF3_1_1	Candida albicans
240         CHS4_1_1         Candida albicans           241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257         GSC1_1_1         Candida albicans           258         GSL1_1_1         Candida albicans	23	38	CHS1_1_1	Candida albicans
241         CHS5_1_1         Candida albicans           242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257         GSC1_1_1         Candida albicans           258         GSL1_1_1         Candida albicans	23	39	CHS2_1_1	Candida albicans
242         CHT1_1_1         Candida albicans           243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257         GSC1_1_1         Candida albicans           258         GSL1_1_1         Candida albicans	24	10	CHS4_1_1	Candida albicans
243         CHT2_1_1         Candida albicans           244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257         GSC1_1_1         Candida albicans           258         GSL1_1_1         Candida albicans	24	11	CHS5_1_1	Candida albicans
244         CHT4_1_1         Candida albicans           245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257         GSC1_1_1         Candida albicans           258         GSL1_1_1         Candida albicans	24	12	CHT1_1_1	Candida albicans
245         CSA1_1_1 1         Candida albicans           246         5triphosphatase_1_1         Candida albicans           247         AAF1_1_1 1         Candida albicans           248         ADH1_1_1         Candida albicans           249         ALS1_1_1         Candida albicans           250         ALS7_1_1         Candida albicans           251         EDT1_1_1         Candida albicans           252         ELF_1_1         Candida albicans           253         ESS1_1_1         Candida albicans           254         FAL1_1_1         Candida albicans           255         GAP1_1_1         Candida albicans           256         GNA1_1_1         Candida albicans           257         GSC1_1_1         Candida albicans           258         GSL1_1_1         Candida albicans	24	13	CHT2_1_1	Candida albicans
246       5triphosphatase_1_1       Candida albicans         247       AAF1_1_1 1       Candida albicans         248       ADH1_1_1       Candida albicans         249       ALS1_1_1       Candida albicans         250       ALS7_1_1       Candida albicans         251       EDT1_1_1       Candida albicans         252       ELF_1_1       Candida albicans         253       ESS1_1_1       Candida albicans         254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	24	14	CHT4_1_1	Candida albicans
247       AAF1_1_1 1       Candida albicans         248       ADH1_1_1       Candida albicans         249       ALS1_1_1       Candida albicans         250       ALS7_1_1       Candida albicans         251       EDT1_1_1       Candida albicans         252       ELF_1_1       Candida albicans         253       ESS1_1_1       Candida albicans         254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	24	15	CSA1_1_1 1	Candida albicans
248       ADH1_1_1       Candida albicans         249       ALS1_1_1       Candida albicans         250       ALS7_1_1       Candida albicans         251       EDT1_1_1       Candida albicans         252       ELF_1_1       Candida albicans         253       ESS1_1_1       Candida albicans         254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	24	16	5triphosphatase_1_1	Candida albicans
249       ALS1_1_1       Candida albicans         250       ALS7_1_1       Candida albicans         251       EDT1_1_1       Candida albicans         252       ELF_1_1       Candida albicans         253       ESS1_1_1       Candida albicans         254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	24	17	AAF1_1_1 1	Candida albicans
250       ALS7_1_1       Candida albicans         251       EDT1_1_1       Candida albicans         252       ELF_1_1       Candida albicans         253       ESS1_1_1       Candida albicans         254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	24	18	ADH1_1_1	Candida albicans
251 EDT1_1_1 Candida albicans 252 ELF_1_1 Candida albicans 253 ESS1_1_1 Candida albicans 254 FAL1_1_1 Candida albicans 255 GAP1_1_1 Candida albicans 256 GNA1_1_1 Candida albicans 257 GSC1_1_1 Candida albicans 258 GSL1_1_1 Candida albicans	24	19	ALS1_1_1	Candida albicans
252       ELF_1_1       Candida albicans         253       ESS1_1_1       Candida albicans         254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	25	50	ALS7_1_1	Candida albicans
253       ESS1_1_1       Candida albicans         254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	25	51	EDT1_1_1	Candida albicans
254       FAL1_1_1       Candida albicans         255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	25	52	ELF_1_1	Candida albicans
255       GAP1_1_1       Candida albicans         256       GNA1_1_1       Candida albicans         257       GSC1_1_1       Candida albicans         258       GSL1_1_1       Candida albicans	25	53	ESS1_1_1	Candida albicans
256 GNA1_1_1 Candida albicans 257 GSC1_1_1 Candida albicans 258 GSL1_1_1 Candida albicans	25	54	FAL1_1_1	Candida albicans
257 GSC1_1_1 Candida albicans 258 GSL1_1_1 Candida albicans	25	55	GAP1_1_1	Candida albicans
258 GSL1_1_1 Candida albicans	25	56	GNA1_1_1	Candida albicans
	25	57	GSC1_1_1	Candida albicans
OFO HIST 1 1 Condide albigane	25	58	GSL1_1_1	Candida albicans
239 MIST_T Calidida abicans	25	59	HIS1_1_1	Candida albicans
260 HTS1_1_1 Candida albicans	26	80	HTS1_1_1	Candida albicans
261 HWP1_2_1 Candida albicans	26	31	HWP1_2_1	Candida albicans
262 HYR1_1_1 Candida albicans	26	62	HYR1_1_1	Candida albicans
263 NT1a_1_1 Candida albicans	26	33	NT1a_1_1	Candida albicans
264 KRE15f_1_1 Candida albicans	26	64	KRE15f_1_1	Candida albicans
265 KRE6_1_1 Candida albicans	26	35	KRE6_1_1	Candida albicans
266 KRE9_1_1 Candida albicans	26	36	KRE9_1_1	Candida albicans
267 MIG1_1_1 Candida albicans	26	§7	MIG1_1_1	Candida albicans

(continued)

	SEQ ID NO	Probe name	Template source
F	268	MLS1_1_1	Candida albicans
5	269	MP65_1_1	Candida albicans
	270	NDE1_1_1	Candida albicans
	271	PFK2_1_1	Candida albicans
10	272	PHR1_1_1	Candida albicans
	273	PHR2_1_1	Candida albicans
	274	PHR3_1_1	Candida albicans
15	275	PRA1_1_1	Candida albicans
	276	PRS1_1_1	Candida albicans
	277	RBT1_1_1	Candida albicans
	278	RBT4_1_1	Candida albicans
20	279	RHO1_1_1	Candida albicans
	280	RNR1_1_1	Candida albicans
	281	RPB7_1_1	Candida albicans
25	282	RPL13_1_1	Candida albicans
	283	RVS167_1_1	Candida albicans
	284	SHA3_1_1	Candida albicans
	285	SKN1_1_1	Candida albicans
30	286	SRB1_1_1	Candida albicans
	287	TCA1_1_1	Candida albicans
	288	TRP1_1_1	Candida albicans
35	289	YAE1_1_1	Candida albicans
	290	YRB1_1_1	Candida albicans
	291	YST1exon2_1_1	Candida albicans
	292	CCN1_1_1	Candida albicans
40	293	CDC28_1_1	Candida albicans
	294	CLN2_1_1	Candida albicans
	295	CPH1_1_1	Candida albicans
45	296	CYB1_1_1	Candida albicans
	297	EFG1_1_1	Candida albicans
	298	MNT1_1_1	Candida albicans
	299	RBF1_1_1	Candida albicans
50	300	RBF1_2_1	Candida albicans
	301	RIM101_1_1	Candida albicans
	302	RIM8_1_1	Candida albicans
55	303	SEC14_1_1	Candida albicans
	304	SEC4_1_1	Candida albicans
	305	TUP1_1_1	Candida albicans

(continued)

	SEQ ID NO	Probe name	Template source
-	306	YPT1_1_1	Candida albicans
5	307	ZNF1CZF1_2_1	Candida albicans
	308	arcA_1_1	Enterococcus faecalis
	309	arcC_1_1	Enterococcus faecalis
10	310	bkdA_1_1	Enterococcus faecalis
	311	cad_1_1	Enterococcus faecalis
	312	camE1_1_1	Enterococcus faecalis
15	313	esrA_1_1	Enterococcus faecalis
	314	dacA_1_1	Enterococcus faecalis
	315	dfr_1_1	Enterococcus faecalis
	316	dhoD1a_1_1	Enterococcus faecalis
20	317	ABC-eltA_1_1	Enterococcus faecalis
	318	agrBfs_1_1	Enterococcus faecalis
	319	agrCfs_1_1	Enterococcus faecalis
25	320	dnaE_1_1	Enterococcus faecalis
	321	ebsA_1_1	Enterococcus faecalis
	322	ebsB_1_1	Enterococcus faecalis
	323	eep_1_1	Enterococcus faecalis
30	324	efaR_1_1	Enterococcus faecalis
	325	gls24_glsB_1_1	Enterococcus faecalis
	326	gph_1_1	Enterococcus faecalis
35	327	gyrAEf_1_1	Enterococcus faecalis
	328	metEf_1_1	Enterococcus faecalis
	329	mntHCb2_1_1	Enterococcus faecalis
	330	mob2_1_1	Enterococcus faecalis
40	331	mvaD_1_1	Enterococcus faecalis
	332	mvaE_1_1	Enterococcus faecalis
	333	parC_1 _1	Enterococcus faecalis
45	334	pcfG_1_1	Enterococcus faecalis
	335	phoZ_1_1	Enterococcus faecalis
	336	polC_1_1	Enterococcus faecalis
	337	ptb_1 _1	Enterococcus faecalis
50	338	reeS1_1_1	Enterococcus faecalis
	339	rpoN_1_1	Enterococcus faecalis
	340	tms_1_1	Enterococcus faecalis
55	341	tyrDC_1_1	Enterococcus faecalis
	342	tyrS_1_1	Enterococcus faecalis
	343	asa1_1_1	Enterococcus faecalis

(continued)

SEQ ID NO	Probe name	Template source
344	asp1_1_1	Enterococcus faecalis
345	cgh_1_1	Enterococcus faecalis
346	cylA_1_1	Enterococcus faecalis
347	cylB_1_1	Enterococcus faecalis
348	cyll_1_1	Enterococcus faecalis
349	cylL_cylS_1_1	Enterococcus faecalis
350	cylM_1_1	Enterococcus faecalis
351	ace_1_1	Enterococcus faecalis
352	ef00108_1_1	Enterococcus faecalis
353	ef00109_1_1	Enterococcus faecalis
354	ef0011_1_1	Enterococcus faecalis
355	ef00113_1_1	Enterococcus faecalis
356	ef0012_1_1	Enterococcus faecalis
357	ef0022_1_1	Enterococcus faecalis
358	ef0031_1_1	Enterococcus faecalis
359	ef0032_1_1	Enterococcus faecalis
360	ef0040_1_1	Enterococcus faecalis
361	ef0058_1_1	Enterococcus faecalis
362	enlA_1_1	Enterococcus faecalis
363	esa_1_1	Enterococcus faecalis
364	esp_1_1	Enterococcus faecalis
365	gelE_1_1	Enterococcus faecalis
366	groEL_1_1	Enterococcus faecalis
367	groES_1_1	Enterococcus faecalis
368	rt1_1_1	Enterococcus faecalis
369	sala_1_1	Enterococcus faecalis
370	salb_1_1	Enterococcus faecalis
371	sea1_1_1	Enterococcus faecalis
372	sep1_1_1	Enterococcus faecalis
373	vicK_1_1	Enterococcus faecalis
374	yycH_1_1	Enterococcus faecalis
375	yycl_1_1	Enterococcus faecalis
376	yycJ_1_1	Enterococcus faecalis
377	bglB_1_1	Enterococcus faecium
378	bgIR_1_1	Enterococcus faecium
379	bglS_1_1	Enterococcus faecium
380	efmA_1_1	Enterococcus faecium
381	efmB_1_1	Enterococcus faecium

(continued)

SEQ ID NO	Probe name	Template source
382	efmC_1_1	Enterococcus faecium
383	mreC_1_1	Enterococcus faecium
384	mreD_1_1	Enterococcus faecium
385	mvaDEfaecium_1_1	Enterococcus faecium
386	mvaEEfaecium_1_1	Enterococcus faecium
387	mvaK1 Efaecium_1_1	Enterococcus faecium
388	mvaK2Efaecium_1_1	Enterococcus faecium
389	mvaSEfaecium_1_1	Enterococcus faecium
390	orf3_4Efaeciumb_1_1	Enterococcus faecium
391	orf6_7Efaecium_1_1	Enterococcus faecium
392	orf7_8Efaecium_1_1	Enterococcus faecium
393	orf9_10Efaecium_1_1	Enterococcus faecium
394	entA_entl_1_1	Enterococcus faecium
395	entD_1_1	Enterococcus faecium
396	entR_1_1	Enterococcus faecium
397	oep_1_1	Enterococcus faecium
398	sagA_1 _2	Enterococcus faecium
399	atsA_1_1	Klebsiella pneumoniae
400	atsB_1_1	Klebsiella pneumoniae
401	budC_1_1	Klebsiella pneumoniae
402	citA_1_1	Klebsiella pneumoniae
403	citW_1_1	Klebsiella pneumoniae
404	citX_1_1	Klebsiella pneumoniae
405	dalD_1_1	Klebsiella pneumoniae
406	dalK_1_1	Klebsiella pneumoniae
407	dalT_1_1	Klebsiella pneumoniae
408	acoA_1 _1	Klebsiella pneumoniae
409	acoB_1 _1	Klebsiella pneumoniae
410	acoC_1_1	Klebsiella pneumoniae
411	ahlK_1_1	Klebsiella pneumoniae
412	fimK_1_1	Klebsiella pneumoniae
413	glfKPN2_1_1	Klebsiella pneumoniae
414	ltrA_1_1	Klebsiella pneumoniae
415	mdcC_1_1	Klebsiella pneumoniae
416	mdcF_1_1	Klebsiella pneumoniae
417	mdcH_1_1	Klebsiella pneumoniae
418	mrkA_1_1	Klebsiella pneumoniae
419	mtrK_1_1	Klebsiella pneumoniae
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SEQ ID NO	Probe name	Template source
420	nifF_1_1	Klebsiella pneumoniae
421	nifK_1_1	Klebsiella pneumoniae
422	nifN_1_1	Klebsiella pneumoniae
423	tyrP_1_1	Klebsiella pneumoniae
424	ureA_1_1	Klebsiella pneumoniae
425	wbbO_1_1	Klebsiella pneumoniae
426	wza_1_1	Klebsiella pneumoniae
427	wzb_1_1	Klebsiella pneumoniae
428	wzm KPN2_1 _1	Klebsiella pneumoniae
429	wztKPN2_1_1	Klebsiella pneumoniae
430	yojH_1_1	Klebsiella pneumoniae
431	liac_1_1	Klebsiella pneumoniae
432	cim_1_1	Klebsiella pneumoniae
433	aldA_1_1	Klebsiella pneumoniae
434	aldA_2_1	Klebsiella pneumoniae
435	hemly_1_1	Klebsiella pneumoniae
436	pSL017_1_1	Klebsiella pneumoniae
437	pSL020_1_1	Klebsiella pneumoniae
438	rcsA_1_1	Klebsiella pneumoniae
439	rmlC_1_1	Klebsiella pneumoniae
440	rmID_1_1	Klebsiella pneumoniae
441	waaG_1_1	Klebsiella pneumoniae
442	wbbD_1_1	Klebsiella pneumoniae
443	wbbM_1_1	Klebsiella pneumoniae
444	wbbN_1_1	Klebsiella pneumoniae
445	wbdA_1 _1	Klebsiella pneumoniae
446	wbdC_1 _1	Klebsiella pneumoniae
447	wztKpn_1_1	Klebsiella pneumoniae
448	yibD_1_1	Klebsiella pneumoniae
449	cymA_1_1	Klebsiella oxytoca
450	cymD_1_1	Klebsiella oxytoca
451	cymE_1_1	Klebsiella oxytoca
452	cymH_1_1	Klebsiella oxytoca
453	cyml_1_1	Klebsiella oxytoca
454	cymd_1_1	Klebsiella oxytoca
455	ddrA_1_1	Klebsiella oxytoca
456	fdt-1_1_1	Klebsiella oxytoca
457	fdt-2_1_1	Klebsiella oxytoca

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SEQ ID NO	Probe name	Template source
458	fdt-3_1_1	Klebsiella oxytoca
459	gatY_1_1	Klebsiella oxytoca
460	hydH_1_1	Klebsiella oxytoca
461	masA_1_1	Klebsiella oxytoca
462	nasA_1_1	Klebsiella oxytoca
463	nasE_1_1	Klebsiella oxytoca
464	nasF_1_1	Klebsiella oxytoca
465	pehX_1_1	Klebsiella oxytoca
466	pelX_1_1	Klebsiella oxytoca
467	tagH_1_1	Klebsiella oxytoca
468	tagK_1_1	Klebsiella oxytoca
469	tagT_1 _1	Klebsiella oxytoca
470	glpR_1_1	Pseudomonas aeruginosa
471	lasRb_1_1	Pseudomonas aeruginosa
472	OrfX_1 _1	Pseudomonas aeruginosa
473	pa0260_1_1	Pseudomonas aeruginosa
474	pa0572_1_1	Pseudomonas aeruginosa
475	pa0625_1_1	Pseudomonas aeruginosa
476	pa0636_1_1	Pseudomonas aeruginosa
477	pa1046_1_1	Pseudomonas aeruginosa
478	pa1069_1_1	Pseudomonas aeruginosa
479	pa1846_1_1	Pseudomonas aeruginosa
480	pa3866_1_1	Pseudomonas aeruginosa
481	pa4082_1_1	Pseudomonas aeruginosa
482	pilAp_1_1	Pseudomonas aeruginosa
483	PilAp2_1_1	Pseudomonas aeruginosa
484	pilC_1_1	Pseudomonas aeruginosa
485	PstP_1_1	Pseudomonas aeruginosa
486	purK_1_1	Pseudomonas aeruginosa
487	uvrDII_1_1	Pseudomonas aeruginosa
488	vsml_1_1	Pseudomonas aeruginosa
489	vsm R_1 _2	Pseudomonas aeruginosa
490	xcpX_1_1	Pseudomonas aeruginosa
491	aprA_1_1	Pseudomonas aeruginosa
492	aprE_1_1	Pseudomonas aeruginosa
493	ctx_1_2	Pseudomonas aeruginosa
494	algB_1_1	Pseudomonas aeruginosa
495	algN_1_1	Pseudomonas aeruginosa

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SEQ ID NO	Probe name	Template source
496	algR_1_1	Pseudomonas aeruginosa
497	ExoS_1_1	Pseudomonas aeruginosa
498	fpvA_1_1	Pseudomonas aeruginosa
499	lasRa_1_1	Pseudomonas aeruginosa
500	lipA_1_1	Pseudomonas aeruginosa
501	lipH_1_1	Pseudomonas aeruginosa
502	Orf159_1_2	Pseudomonas aeruginosa
503	Orf252_1_1	Pseudomonas aeruginosa
504	pchG_1_1	Pseudomonas aeruginosa
505	PhzA_1_1	Pseudomonas aeruginosa
506	PhzB_1_1	Pseudomonas aeruginosa
507	PLC_1_1	Pseudomonas aeruginosa
508	plcN_1_1	Pseudomonas aeruginosa
509	plcR_1_1	Pseudomonas aeruginosa
510	pvdD_1_1	Pseudomonas aeruginosa
511	pvdF_1_2	Pseudomonas aeruginosa
512	pyocinS1_1_1	Pseudomonas aeruginosa
513	pyocinS1im_1_1	Pseudomonas aeruginosa
514	pyocinS2_1_1	Pseudomonas aeruginosa
515	pys2_1_1	Pseudomonas aeruginosa
516	pys2_2_1	Pseudomonas aeruginosa
517	rbf303_1_1	Pseudomonas aeruginosa
518	rhIA_1_1	Pseudomonas aeruginosa
519	rhlB_1_1	Pseudomonas aeruginosa
520	rhIR_1_1	Pseudomonas aeruginosa
521	TnAP41_1_2	Pseudomonas aeruginosa
522	toxA_1_1	Pseudomonas aeruginosa
523	cap1EStrpneu_1_1	Streptococcus pneumoniae
524	cap1FStrpneu_1_1	Streptococcus pneumoniae
525	cap1GStrpneu_1_1	Streptococcus pneumoniae
526	cap3AStrpneu_1_1	Streptococcus pneumoniae
527	cap3BStrpneu_1_1	Streptococcus pneumoniae
528	celAStrpneu_1_1	Streptococcus pneumoniae
529	celBStrpneu_1_1	Streptococcus pneumoniae
530	cglAStrpneu_1_1	Streptococcus pneumoniae
531	cglBStrpneu_1_1	Streptococcus pneumoniae
532	cglCStrpneu_1_1	Streptococcus pneumoniae
533	cglDStrpneu_1_1	Streptococcus pneumoniae

(continued)

SEQ ID NO	Probe name	Template source
534	cinA_1_1	Streptococcus pneumoniae
535	cps14EStrpneum_1_1	Streptococcus pneumoniae
536	cps14FStrpneum_1_1	Streptococcus pneumoniae
537	cps14GStrpneum_1_1	Streptococcus pneumoniae
538	cps14HStrpneum_1_1	Streptococcus pneumoniae
539	cps19aHStrpneum_1_1	Streptococcus pneumoniae
540	cps19alStrpneum_1_1	Streptococcus pneumoniae
541	cps19aKStrpneum_1_1	Streptococcus pneumoniae
542	cps19fGStrpneum_1_1	Streptococcus pneumoniae
543	cps23fGStrpneum_1_1	Streptococcus pneumoniae
544	dexB_1_1	Streptococcus pneumoniae
545	dinF_1_1	Streptococcus pneumoniae
546	1760Strpneu_1_1	Streptococcus pneumoniae
547	acyPStrpneu_1_1	Streptococcus pneumoniae
548	endAStrpneu_1 _1	Streptococcus pneumoniae
549	exoAStrpneu_1_1	Streptococcus pneumoniae
550	exp72_1_1	Streptococcus pneumoniae
551	fnIAStrpneu_1_1	Streptococcus pneumoniae
552	fnlBStrpneu_1_1	Streptococcus pneumoniae
553	fnlCStrpneu_1_1	Streptococcus pneumoniae
554	gct18Strpneum_1_1	Streptococcus pneumoniae
555	hexB1_1_1	Streptococcus pneumoniae
556	hftsHstrpneu_1_1	Streptococcus pneumoniae
557	immunofrag 1 Strpneu_1_1	Streptococcus pneumoniae
558	immunofrag2Strpneu_2_1	Streptococcus pneumoniae
559	immunofrag3Strpneu_2_1	Streptococcus pneumoniae
560	kdtBStrpneu_1_1	Streptococcus pneumoniae
561	lysAStrpneu_1_1	Streptococcus pneumoniae
562	pcpBStrpneu_1_1	Streptococcus pneumoniae
563	pflCStrpneu_1_1	Streptococcus pneumoniae
564	plpA_1_1	Streptococcus pneumoniae
565	prtAlStrpneu_1_1	Streptococcus pneumoniae
566	pspC1Strpneu_1 _1	Streptococcus pneumoniae
567	pspC2_1_1	Streptococcus pneumoniae
568	purRStrpneu_1_1	Streptococcus pneumoniae
569	pyrDAStrpneum_1_1	Streptococcus pneumoniae
570	SP0828Strpneu_1_1	Streptococcus pneumoniae
571	SP0830Strpneu_1_1	Streptococcus pneumoniae

(continued)

SEQ ID NO	Probe name	Template source
572	SP0833Strpneu_1_1	Streptococcus pneumoniae
573	SP0837_38Strpneu_1_1	Streptococcus pneumoniae
574	SP0839Strpneu_1_1	Streptococcus pneumoniae
575	ugdStrpneu_1_1	Streptococcus pneumoniae
576	uncC_1_1	Streptococcus pneumoniae
577	vicXStrepneu_1_1	Streptococcus pneumoniae
578	wchA6bStrpneum_1_1	Streptococcus pneumoniae
579	wci4Strpneum_1_1	Streptococcus pneumoniae
580	wciK4Strpneum_1_1	Streptococcus pneumoniae
581	wciL4Strpneum_1_1	Streptococcus pneumoniae
582	wciN6bStrpneum_1_1	Streptococcus pneumoniae
583	wciO6bStrpneum_1_1	Streptococcus pneumoniae
584	wciP6bStrpneum_1_1	Streptococcus pneumoniae
585	wciY18Strpneum_1_1	Streptococcus pneumoniae
586	wzdbStrpneum_1_1	Streptococcus pneumoniae
587	wze6bStrpneum_1_1	Streptococcus pneumoniae
588	wzy18Strpneum_1_1	Streptococcus pneumoniae
589	wzy4Strpneum_1_1	Streptococcus pneumoniae
590	wzy6bStrpneum_1_1	Streptococcus pneumoniae
591	xpt_1_1	Streptococcus pneumoniae
592	igaStrpneu_1_1	Streptococcus pneumoniae
593	lytA_1_1	Streptococcus pneumoniae
594	nanA_1 _1	Streptococcus pneumoniae
595	nanBStrpneu_1_1	Streptococcus pneumoniae
596	pcpCStrpneu_1_1	Streptococcus pneumoniae
597	ply_1_1	Streptococcus pneumoniae
598	prtAStrpneu_1_1	Streptococcus pneumoniae
599	pspA_1 _2	Streptococcus pneumoniae
600	SP0834Strpneu_1_1	Streptococcus pneumoniae
601	SP0834Strpneu_1_2	Streptococcus pneumoniae
602	sphtraStrpneu_1_1	Streptococcus pneumoniae
603	wciJStrpneu_1_1	Streptococcus pneumoniae
604	wziyStrpneu_1_1	Streptococcus pneumoniae
605	wzxStrpneu_1_1	Streptococcus pneumoniae
606	cpsA1Strgal_1_1	Streptococcus agalactiae
607	cpsB1 Strgal_1_1	Streptococcus agalactiae
608	cpsC1Strgal_1_1	Streptococcus agalactiae
609	cpsD1Strgal_1_1	Streptococcus agalactiae

(continued)

SEQ ID NO	Probe name	Template source
610	cpsE1Strgal_1_1	Streptococcus agalactiae
611	cpsG1Strgal_1_1	Streptococcus agalactiae
612	cpslStragal_1_1	Streptococcus agalactiae
613	cpsJStragal_1_1	Streptococcus agalactiae
614	cpsKStragal_1_1	Streptococcus agalactiae
615	cpsMStragal_1_1	Streptococcus agalactiae
616	cpsYStragal_1_1	Streptococcus agalactiae
617	cpsYStragal_2_1	Streptococcus agalactiae
618	cylBStraga_1_1	Streptococcus agalactiae
619	cylEStraga_1_1	Streptococcus agalactiae
620	cylFStraga_1_1	Streptococcus agalactiae
621	cylHStraga_1_1	Streptococcus agalactiae
622	cyllStraga_1_1	Streptococcus agalactiae
623	cylJStraga_1_1	Streptococcus agalactiae
624	cylKStraga_1_1	Streptococcus agalactiae
625	0487Straga_1_1	Streptococcus agalactiae
626	0488Straga_1_1	Streptococcus agalactiae
627	0493Straga_1_1	Streptococcus agalactiae
628	0495Straga_1_1	Streptococcus agalactiae
629	0498Straga_1_1	Streptococcus agalactiae
630	0500Straga_1_1	Streptococcus agalactiae
631	0502Straga_1_1	Streptococcus agalactiae
632	0504Straga_1_1	Streptococcus agalactiae
633	folDStraga_1_1	Streptococcus agalactiae
634	neuA1Strgal_1_1	Streptococcus agalactiae
635	neuB1Strgal_1_1	Streptococcus agalactiae
636	neuC1Strgal_1_1	Streptococcus agalactiae
637	neuD1Strgal_1_1	Streptococcus agalactiae
638	recNStraga_1_1	Streptococcus agalactiae
639	ileSStraga_1_1	Streptococcus agalactiae
640	CAMPfactor_1_1	Streptococcus agalactiae
641	CAMPfactor_2_1	Streptococcus agalactiae
642	0499Straga_1_1	Streptococcus agalactiae
643	hylStragal_1_1	Streptococcus agalactiae
644	lipStragal_1_1	Streptococcus agalactiae
645	cyclStrpyog_1_1	Streptococcus pyogenes
		0
646	fah_rph_hlo_Strpyog_1_1	Streptococcus pyogenes

(continued)

SEQ ID NO	Probe name	Template source
648	int315.5_1_1	Streptococcus pyogenes
649	murEStrpyog_1_1	Streptococcus pyogenes
650	oppA_1_1	Streptococcus pyogenes
651	oppCStrpyog_1_1	Streptococcus pyogenes
652	oppD_1_1	Streptococcus pyogenes
653	SPy0382Strpyog_1_1	Streptococcus pyogenes
654	SPy0390Strpyog_1_1	Streptococcus pyogenes
655	SpyM3_1351_1_1	Streptococcus pyogenes
656	vicXStrpyog_1_1	Streptococcus pyogenes
657	DNaselStrpyog_1_1	Streptococcus pyogenes
658	fba2Strpyog_1_1	Streptococcus pyogenes
659	fhuAStrpyog_1_1	Streptococcus pyogenes
660	fhuBiStrpyog_1_1	Streptococcus pyogenes
661	fhuDStrpyog_1_1	Streptococcus pyogenes
662	fhuGStrpyog_1_1	Streptococcus pyogenes
663	hylA_1_1	Streptococcus pyogenes
664	hyIP_1_1	Streptococcus pyogenes
665	hylp2_1_1	Streptococcus pyogenes
666	oppB_1_1	Streptococcus pyogenes
667	ropB_1 _1	Streptococcus pyogenes
668	scpAStrpyog_1_1	Streptococcus pyogenes
669	sloStrpyog_1_1	Streptococcus pyogenes
670	smez-4Strpyog_1_1	Streptococcus pyogenes
671	sof_1_1	Streptococcus pyogenes
672	sof_2_1	Streptococcus pyogenes
673	speA_1_1	Streptococcus pyogenes
674	speB2Strpyog_1_1	Streptococcus pyogenes
675	speCStrpyog_1 _1	Streptococcus pyogenes
676	speJStrpyog_1_1	Streptococcus pyogenes
677	srtBStrpyog_1_1	Streptococcus pyogenes
678	srtCStrpyog_1_1	Streptococcus pyogenes
679	srtEStrpyog_1_1	Streptococcus pyogenes
680	srtFStrpyog_1_1	Streptococcus pyogenes
681	srtGStrpyog_1_1	Streptococcus pyogenes
682	srtlStrpyog_1_1	Streptococcus pyogenes
683	srtKStrpyog_1_1	Streptococcus pyogenes
684	srtRStrpyog_1_1	Streptococcus pyogenes
685	srtTStrpyog_1_1	Streptococcus pyogenes

(continued)

SEQ ID NO	Probe name	Template source
686	vicKStrpyog_1_1	Streptococcus pyogenes
687	573Stprmut_1_1	Streptococcus viridans
688	580SStprm ut_1 _1	Streptococcus viridans
689	581_582SStprmut_1_1	Streptococcus viridans
690	584SStprmut_1_1	Streptococcus viridans
691	dltAStrmut_1_1	Streptococcus viridans
692	dltBStrmut_1_1	Streptococcus viridans
693	dltCppx1Strmut_1_1	Streptococcus viridans
694	dltDStrmut_1_1	Streptococcus viridans
695	lichStrbov_1_1	Streptococcus viridans
696	lytRStprmut_1_1	Streptococcus viridans
697	lytSStprmut_1_1	Streptococcus viridans
698	pepQStrrmut_1_1	Streptococcus viridans
699	pflCStrmut_1_1	Streptococcus viridans
700	recNStprmut_1_1	Streptococcus viridans
701	ytqBStrmut_1_1	Streptococcus viridans
702	hlyXStrmut_1_1	Streptococcus viridans
703	igaStrmitis_1_1	Streptococcus viridans
704	igaStrsanguis_1_1	Streptococcus viridans
705	perMStrmut_1_1	Streptococcus viridans
706	atfA_1_1	Proteus mirabilis
707	atfB_1_1	Proteus mirabilis
708	atfC_1_1	Proteus mirabilis
709	ccmPrmi1_1_1	Proteus mirabilis
710	cyaPrmi_1_1	Proteus mirabilis
711	aad_1_1	Proteus mirabilis
712	flfB_1_1	Proteus mirabilis
713	flfD_1_1	Proteus mirabilis
714	flfN_1_1	Proteus mirabilis
715	flhD_1_1	Proteus mirabilis
716	floA_1_1	Proteus mirabilis
717	ftsK_1_1	Proteus mirabilis
718	gstB_1_1	Proteus mirabilis
719	hem CPrmi_1_1	Proteus mirabilis
720	hem DPrmi_1_1	Proteus mirabilis
721	hev_1_1	Proteus mirabilis
722	katA_1_1	Proteus mirabilis
723	lpp1_1_1	Proteus mirabilis

(continued)

	SEQ ID NO	Probe name	Template source
E	724	menE_1_1	Proteus mirabilis
5	725	mfd_1_1	Proteus mirabilis
	726	nrpA_1_1	Proteus mirabilis
	727	nrpB_1_1	Proteus mirabilis
10	728	nrpG_1_1	Proteus mirabilis
	729	nrpS_1_1	Proteus mirabilis
	730	nrpT_1_1	Proteus mirabilis
15	731	nrpU_1_1	Proteus mirabilis
	732	pat_1_1	Proteus mirabilis
	733	pmfA_1_1	Proteus mirabilis
	734	pmfC_1_1	Proteus mirabilis
20	735	pmfE_1_1	Proteus mirabilis
	736	ppaA_1_1	Proteus mirabilis
	737	rsbA_1_1	Proteus mirabilis
25	738	rsbC_1_1	Proteus mirabilis
	739	speB_1_1	Proteus mirabilis
	740	stmA_1_1	Proteus mirabilis
	741	stmB_1_1	Proteus mirabilis
30	742	terA_1_1	Proteus mirabilis
	743	terD_1_1	Proteus mirabilis
	744	umoA_1_1	Proteus mirabilis
35	745	umoB_1_1	Proteus mirabilis
	746	umoC_1_1	Proteus mirabilis
	747	ureR_1_1	Proteus mirabilis
	748	xerC_1_1	Proteus mirabilis
40	749	ygbA_1_1	Proteus mirabilis
	750	flaA_1_1	Proteus mirabilis
	751	flaD_1_1	Proteus mirabilis
45	752	fliA_1_1	Proteus mirabilis
	753	hpmA_1_1	Proteus mirabilis
	754	hpmB_1_1	Proteus mirabilis
	755	lpsPrmi_1_1	Proteus mirabilis
50	756	mrpA_1_1	Proteus mirabilis
	757	mrpB_1_1	Proteus mirabilis
	758	mrpC_1_1	Proteus mirabilis
55	759	mrpD_1_1	Proteus mirabilis
	760	mrpE_1_1	Proteus mirabilis
	761	mrpF_1_1	Proteus mirabilis

(continued)

SEQ ID NO	Probe name	Template source
762	mrpG_1_1	Proteus mirabilis
763	mrpH_1_1	Proteus mirabilis
764	mrpl_1_1	Proteus mirabilis
765	mrpJ_1_1	Proteus mirabilis
766	patA_1_1	Proteus mirabilis
767	putA_1_1	Proteus mirabilis
768	uca_1_1	Proteus mirabilis
769	ureDPrmi_1_1	Proteus mirabilis
770	ureEPrmi_1_1	Proteus mirabilis
771	ureFPrmi_1_1	Proteus mirabilis
772	zapA_1_1	Proteus mirabilis
773	zapB_1_1	Proteus mirabilis
774	zapD_1_1	Proteus mirabilis
775	zapE_1_1	Proteus mirabilis
776	envZPrvu_1_1	Proteus vulgaris
777	frdC_1_1	Proteus vulgaris
778	frdD_1_1	Proteus vulgaris
779	infBPrvu_1 _1	Proteus vulgaris
780	lad_1_1	Proteus vulgaris
781	tna2_1_1	Proteus vulgaris
782	end_1 _1	Proteus vulgaris
783	pqrA_1_1	Proteus vulgaris
784	urg_1_1	Proteus vulgaris
785	blaIMP-7_1_1	Pseudomonas aeruginosa
786	meclSepid_1_1	Staphylococcus epidermidis
787	blaOXA-10_1_2	Pseudomonas aeruginosa
788	blaB_1_1	Proteus vulgaris
789	ampC_1_1	Klebsiella oxytoca
790	I-blaR_1_1	Staphylococcus aureus
791	blaOXA-32_1_1	Pseudomonas aeruginosa
792	bla- CTX-M-22_1_1	Klebsiella pneumoniae
793	pbp2aStrpneu_1_1	Streptococcus pneumoniae
794	blaSHV-1_1_1	Klebsiella pneumoniae
795	blaOXA-2_1_1	Salmonella typhimurium
796	blaRShaemolyt_1_1	Staphylococcus haemolyticus
797	blaIMP-7_1_2	Pseudomonas aeruginosa
798	I-mecR_1_1	Staphylococcus aureus
799	blaOXY_1_1	Klebsiella oxytoca

(continued)

	SEQ ID NO	Probe name	Template source
	800	dacCStrpyog_1_1	Streptococcus pyogenes
	801	femA_1_1	Staphylococcus aureus
	802	mecA_1_1	Staphylococcus aureus
	803	blalShaemolyt_1_1	Staphylococcus haemolyticus
	804	blavim_1_1	Pseudomonas aeruginosa
	805	pbp2b_1 _1	Streptococcus pneumoniae
	806	pbp2primeSepid_1_1	Staphylococcus epidermidis
	807	pbp2x_1_1	Streptococcus pneumoniae
	808	pbp3Saureuc_1_1	Staphylococcus aureus
	809	pbp4_1_1	Enterococcus faecalis
	810	pbp5Efaecium_1_1	Enterococcus faecium
	811	pbpC_1_1	Enterococcus faecalis
	812	I-mecl_1_1	Staphylococcus aureus
	813	pbp1a_1_1	Streptococcus pneumoniae
	814	l-blal_1_1	Staphylococcus aureus
	815	blaTEM-106_1_1	Escherichia coli
	816	blaOXY-KLOX_1_1	Klebsiella oxytoca
	817	ftsWEF_1_1	Enterococcus faecium
	818	fmhB_1_1	Staphylococcus aureus
	819	cumA_1_1	Proteus vulgaris
	820	femBShaemolyt_1_1	Staphylococcus haemolyticus
	821	blaPER-1_1_1	Pseudomonas aeruginosa
	822	bla_FOX-3_1_1	Klebsiella oxytoca
	823	blaA_1_1	Proteus vulgaris
	824	psrb_1_1	Enterococcus faecium
	825	fmhA_1_1	Staphylococcus aureus
	826	mecR1Sepid_1_1	Staphylococcus epidermidis
	827	blaZ_1 _1	Staphylococcus aureus
	828	blaOXA-1_1_1	Plasmid FGN238
	829	fox-6_1_1	Klebsiella pneumoniae
	830	b!aPrmi_1_1	Proteus mirabilis
	831	aacA_aphDStwar_1_1	Staphylococcus warneri
	832	aacC1_1_2	Pseudomonas aeruginosa
	833	aacC2_1_1	Escherichia coli
	834	strB_1_1	Escherichia coli
	835	aadA_1_1	Enterococcus faecalis
	836	aadB_1_2	Escherichia coli
	837	aadD_1_1	Staphylococcus aureus
!			

(continued)

SEQ ID NO	Probe name	Template source
838	aacA4_1_2	Pseudomonas aeruginosa
839	strA_1_1	Escherichia coli
840	aph-A3_1_1	Staphylococcus aureus
841	aacC1_1_1	Pseudomonas aeruginosa
842	aacA4_1_1	Pseudomonas aeruginosa
843	aacA-aphD_1_1	Staphylococcus aureus
844	I-spc_1_1	Staphylococcus aureus
845	aphA3_1_1	synthetic construct
846	ermC_1_1	Staphylococcus aureus
847	linB_1_1	Enterococcus faecium
848	satSA_1_1	Staphylococcus aureus
849	mdrSA_1_1	Staphylococcus aureus
850	I-linA_1_1	Staphylococcus aureus
851	erm B_1 _2	Staphylococcus aureus
852	ermA_1_1	Staphylococcus aureus
853	satA_1_1	Enterococcus faecium
854	msrA_1_1	Staphylococcus aureus
855	mphBM_1_1	Staphylococcus aureus
856	mefA_1_1	Streptococcus pyogenes
857	mrx_1_1	Escherichia coli
858	dfrStrpneu_1 _1	Streptococcus pneumoniae
859	dfrA_1_1	Staphylococcus aureus
860	cm IA5_1_1	Escherichia coli
861	catEfaecium_1_1	Enterococcus faecium
862	cat_1 _1	Staphylococcus aureus
863	tetAJ_1_1	Proteus mirabilis
864	tetL_1_1	Enterococcus faecalis
865	tetM_1_1	Enterococcus faecalis
866	vanH(tn)_1_1	Enterococcus faecium
867	vanA_1_1	Enterococcus faecium
868	vanHB2_1_1	Enterococcus faecium
869	vanR_1_1	Enterococcus faecium
870	vanRB2_1_1	Enterococcus faecium
871	vanS(tn)_1_1	Enterococcus faecium
872	vanSB2_1_1	Enterococcus faecium
873	vanWB2_1_1	Enterococcus faecium
874	ddl_1_1	Enterococcus faecalis
875	ble_1_1	Staphylococcus aureus

(continued)

SEQ ID NO	Probe name	Template source
876	vanXB2_1_1	Enterococcus faecium
877	vanY(tn)_1_1	Enterococcus faecium
878	vanYB2_1_1	Enterococcus faecium
879	vanB_1_1	Enterococcus faecalis
880	vanZ(tn)_1_1	Enterococcus faecium
881	vanC-2_1_1	Enterococcus flavescens
882	vanX(tn)_1_1	Enterococcus faecium
883	acrB_1_1	Proteus mirabilis
884	mexB_1_2	Pseudomonas aeruginosa
885	I-qacA_1_1	Staphylococcus aureus
886	sull_1_1	Escherichia coli
887	sul_1_1	Escherichia coli
888	cadBStalugd_1_1	Staphylococcus lugdunensis
889	mexA_1_1	Pseudomonas aeruginosa
890	acrR_1_1	Proteus mirabilis
891	emeA_1_1	Enterococcus faecalis
892	acrA_1_1	Proteus mirabilis
893	rtn_1_1	Proteus vulgaris
894	abcXStrpmut_1_1	Streptococcus mutans
895	qacEdelta1_1 _1	Escherichia coli
896	elkT-abcA_1_1	Staphylococcus aureus
897	I-cadA_1_1	Staphylococcus aureus
898	albA_1_1	Klebsiella oxytoca
899	wzm_1_1	Klebsiella pneumoniae
900	msrCb_1_1	Enterococcus faecium
901	nov_1_1	Escherichia coli
902	wzt_1_1	Klebsiella pneumoniae
903	wbbl_1_1	Klebsiella pneumoniae
904	norA23_1_1	Staphylococcus aureus
905	mexR_1_1	Pseudomonas aeruginosa
906	arr2_1_1	Escherichia coli
907	mreA_1_1	Staphylococcus aureus
908	I-cadC_1_1	Staphylococcus aureus
909	uvrA_1_1	Enterococcus faecalis
910	CRD2_1_1	Candida albicans
911	CDR1_1_1	Candida albicans
912	CDR1_2_1	Candida albicans
913	MET3_1_1	Candida albicans

(continued)

	SEQ ID NO	Probe name	Template source
5	914	FET3_1 _1	Candida albicans
5	915	FTR2_1_1	Candida albicans
	916	MDR1-7_1_1	Candida albicans
	917	ERG11_1_1	Candida albicans
10	918	SEC20_1_1	Candida albicans
	919	rbcL_1_1	Glycine max
	920	LDHA(hu)_1_1	Homo sapiens
15	921	GAPD(hu)_1_1	Homo sapiens
	922	b-Act(hu)_1_1	Homo sapiens
	923	ARHGDIA(hu)_1_1	Homo sapiens
	924	PGK1(hu)_1_1	Homo sapiens
20	925	rbcL_1_2	Glycine max
	926	16SPa_1_1	Pseudomonas aeruginosa
	927	23SEfaecium_2_1	Enterococcus faecium
25	928	16SStrepyog_1_1	Streptococcus pyogenes
	929	16SStrepneu_1_1	Streptococcus pneumoniae
	930	16SStrepagalactiae_1_1	Streptococcus agalactiae
	931	16SEfaecium_1_1	Enterococcus faecium
30	932	16SEfaecium_2_1	Enterococcus faecium
	933	16SRNAEf_2_1	Enterococcus faecalis
	934	16SKpn_1_1	Klebsiella pneumoniae
35	935	16SSa_3_1	Staphylococcus aureus
	936	16SRNAEf_1_1	Enterococcus faecalis
	937	16SShominis_1_1	Staphylococcus hominis
	938	16SShaemolyt_1_1	Staphylococcus haemolyticus
40	939	23SEfaecium_1_1	Enterococcus faecium
	940	16SrRNAPrmi_1_1	Proteus mirabilis
	941	16SrRNAPrvu1_1_1	Proteus vulgaris
45	942	16SSa_1_1	Staphylococcus aureus
	943	16SKlox_1_1	Klebsiella oxytoca
	944	p53_1_1	Mus musculus
	945	0135mihck_1_1	Dictyostelium discoideum
50	946	FAN_1_1	Mus musculus
	947	0270cap_1 _1	Dictyostelium discoideum

b) primer sequences

	SEQ ID NO	Probe name	Direction
	948	cataSaur_1_1	F(orward)
5	949	cataSaur_1_1	R(everse)
ŭ	950	cataSaur_1_2	F
	951	cataSaur_1_2	R
	952	clfA_1_1	F
10	953	clfA_1_1	R
	954	clfB_1_1	F
	955	clfB_1_1	R
15	956	coa_1_1	F
	957	coa_1_1	R
	958	coa_1_2	F
	959	coa_1_2	R
20	960	I-clpC_1_1	F
	961	I-clpC_1_1	R
	962	I-clpP_1_1	F
25	963	I-clpP_1_1	R
	964	I-ctaA_1_1	F
	965	I-ctaA_1_1	R
	966	I-ctsR_1_1	F
30	967	I-ctsR_1_1	R
	968	I-dltA_1_1	F
	969	I-dltA_1_1	R
35	970	I-dltB_1_1	F
	971	I-dltB_1_1	R
	972	I-dltC_1_1	F
	973	I-dltc_1_1	R
40	974	I-dnaK_1_1	F
	975	I-dnaK_1_1	R
	976	I-elkT_1_1	F
45	977	I-elkT_1_1	R
	978	I-femD_1_1	F
	979	I-femD_1_1	R
	980	I-glnA_1 _1	F
50	981	l-glnA_1_1	R
	982	I-glnR_1_1	F
	983	I-glnR_1_1	R
55	984	I-grlA_1_1	F
	985	I-grlA_1_1	R
	986	I-grlB_1_1	F

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	SEQ ID NO	Probe name	Direction
5	987	I-grlB_1_1	R
	988	I-groEL_1_1	F
	989	I-groEL_1_1	R
	990	I-groES_1_1	F
10	991	I-groES_1_1	R
	992	I-hemA_1_1	F
	993	I-hemA_1_1	R
15	994	I-hemE_1_1	F
10	995	I-hemE_1_1	R
	996	I-hemH_1_1	F
	997	I-hemH_1_1	R
20	998	I-hemL_1_1	F
	999	I-hemL_1_1	R
	1000	I-hemY_1_1	F
25	1001	I-hemY_1_1	R
	1002	I-lepA_1 _1	F
	1003	I-lepA_1 _1	R
	1004	I-lrgA_1_1	F
30	1005	I-lrgA_1_1	R
	1006	I-lrgB_1_1	F
	1007	I-lrgB_1_1	R
35	1008	I-lytM_1_1	F
	1009	I-lytM_1_1	R
	1010	I-menB_1_1	F
	1011	I-menB_1_1	R
40	1012	I-menD_1_1	F
	1013	I-menD_1_1	R
	1014	I-menE_1_1	F
45	1015	I-menE_1_1	R
	1016	I-menF_1_1	F
	1017	I-menF_1_1	R
	1018	I-mreB_1_1	F
50	1019	I-mreB_1_1	R
	1020	I-mreR_1_1	F
	1021	I-mreR_1_1	R
55	1022	I-mutL_1_1	F
	1023	I-mutL_1_1	R
	1024	I-mutS_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1025	I-mutS_1_1	R
	1026	I-NAG_1_1	F
	1027	I-NAG_1_1	R
	1028	I-pbg_1_1	F
10	1029	I-pbg_1_1	R
	1030	I-pbpF_1_1	F
	1031	I-pbpF_1_1	R
15	1032	I-pdhB_1_1	F
	1033	I-pdhB_1_1	R
	1034	I-pdhC_1_1	F
	1035	I-pdhC_1_1	R
20	1036	I-rsbU_1_1	F
	1037	I-rsbU_1_1	R
	1038	I-rsbV_1_1	F
25	1039	I-rsbV_1_1	R
	1040	I-rsbW_1_1	F
	1041	I-rsbW_1_1	R
	1042	I-sgp_1_1	F
30	1043	I-sgp_1_1	R
	1044	I-sirR_1_1	F
	1045	I-sirR_1_1	R
35	1046	I-sodA_1_1	F
	1047	I-sodA_1_1	R
	1048	I-sodB_1_1	F
	1049	I-sodB_1_1	R
40	1050	I-sstA_1_1	F
	1051	I-sstA_1_1	R
	1052	I-sstB_1_1	F
45	1053	I-sstB_1_1	R
	1054	I-sstC_1_1	F
	1055	I-sstC_1_1	R
	1056	I-sstD_1_1	F
50	1057	I-sstD_1_1	R
	1058	I-trx_1_1	F
	1059	I-trx_1_1	R
55	1060	l-yhiN_1_1	F
	1061	l-yhiN_1_1	R
	1062	epiP-bsaP_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1063	epiP-bsaP_1_1	R
3	1064	geh_1_1	F
	1065	geh_1_1	R
	1066	gyrA_1_1	F
10	1067	gyrA_1_1	R
	1068	gyrB_1_1	F
	1069	gyrB_1_1	R
15	1070	hemB_1_1	F
	1071	hemB_1_1	R
	1072	hemC_1_1	F
	1073	hemC_1_1	R
20	1074	hemD_1_1	F
	1075	hemD_1_1	R
	1076	hemN_1_1	F
25	1077	hemN_1_1	R
	1078	hsdS_1_1	F
	1079	hsdS_1_1	R
	1080	hsdS_2_1	F
30	1081	hsdS_2_1	R
	1082	lip_1 _1	F
	1083	lip_1_1	R
35	1084	menC_1_1	F
	1085	menC_1_1	R
	1086	murC_1_1	F
	1087	murC_1_1	R
40	1088	nuc_1_1	F
	1089	nuc_1_1	R
	1090	pdhD_1_1	F
45	1091	pdhD_1_1	R
	1092	rpoB_1_1	F
	1093	rpoB_1_1	R
	1094	SAV0431_1_1	F
50	1095	SAV0431_1_1	R
	1096	SAV0439_1_1	F
	1097	SAV0439_1_1	R
55	1098	SAV0440_1_1	F
	1099	SAV0440_1_1	R
	1100	SAV0441_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1101	SAV0441_1_1	R
	1102	sigB_1_1	F
	1103	sigB_1_1	R
	1104	spa_1_2	F
10	1105	spa_1_2	R
	1106	sstC_1_1	F
	1107	sstC_1_1	R
15	1108	tag_1_1	F
	1109	tag_1_1	R
	1110	tyrA_1_1	F
	1111	tyrA_1_1	R
20	1112	I-aroC_1_1	F
	1113	I-aroC_1_1	R
	1114	I-aroA_1_1	F
25	1115	I-aroA_1_1	R
	1116	I-cna_1_1	F
	1117	I-cna_1_1	R
	1118	I-ebpS_1_1	F
30	1119	I-ebpS_1_1	R
	1120	I-eno_1_1	F
	1121	I-eno_1_1	R
35	1122	I-fbpA_1_1	F
	1123	I-fbpA_1_1	R
	1124	I-fib_1_1	F
	1125	I-fib_1_1	R
40	1126	I-fnbB_1_1	F
	1127	I-fnbB_1_1	R
	1128	I-srtA_1_1	F
45	1129	I-srtA_1_1	R
	1130	I-stpC_1_1	F
	1131	I-stpC_1_1	R
	1132	I-fnbA_1_1	F
50	1133	I-fnbA_1_1	R
	1134	I-spa_1_1	F
	1135	I-spa_1_1	R
55	1136	I-aroE_1_1	F
	1137	I-aroE_1_1	R
	1138	I-aroF_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1139	I-aroF_1_1	R
	1140	I-aroG_1_1	F
	1141	I-aroG_1_1	R
	1142	I-asp23_1_1	F
10	1143	I-asp23_1_1	R
	1144	I-atl_1_1	F
	1145	I-atl_1_1	R
15	1146	bsaE_1_1	F
	1147	bsaE_1_1	R
	1148	bsaG_1_1	F
	1149	bsaG_1_1	R
20	1150	cap5h_1_1	F
	1151	cap5h_1_1	R
	1152	cap5i_1_1	F
25	1153	cap5i_1_1	R
	1154	cap5j_1_1	F
	1155	cap5j_1_1	R
	1156	cap5k_1_1	F
30	1157	cap5k_1_1	R
	1158	capBH_1_1	F
	1159	cap8H_1_1	R
35	1160	cap8l_1_1	F
	1161	cap8l_1_1	R
	1162	cap8J_1_1	F
	1163	cap8J_1_1	R
40	1164	cap8K_1_1	F
	1165	cap8K_1_1	R
	1166	I-hld_1_1	F
45	1167	I-hld_1_1	R
	1168	I-hysA_1_1	F
	1169	I-hysA_1_1	R
	1170	I-lgGbg_1_1	F
50	1171	I-lgGbg_1_1	R
	1172	EDIN_1_1	F
	1173	EDIN_1_1	R
55	1174	eta_1_1	F
	1175	eta_1_1	R
	1176	etb_1_1	F

	SEQ ID NO	Probe name	Direction
5	1177	etb_1_1	R
3	1178	hglA_1_1	F
	1179	hglA_1_1	R
	1180	hglA_2_1	F
10	1181	hglA_2_1	R
	1182	hglB_1_1	F
	1183	hglB_1_1	R
15	1184	hglC_2_1	F
	1185	hglC_2_1	R
	1186	hla_1_1	F
	1187	hla_1_1	R
20	1188	hlb_1_2	F
	1189	hlb_1_2	R
	1190	lukF_1_1	F
25	1191	lukF_1_1	R
	1192	lukS_1_1	F
	1193	lukS_1_1	R
	1194	lukS_2_1	F
30	1195	lukS_2_1	R
	1196	NAG_1_1	F
	1197	NAG_1_1	R
35	1198	sak_1_1	F
	1199	sak_1_1	R
	1200	sea_1_1	F
	1201	sea_1_1	R
40	1202	seb_1_1	F
	1203	seb_1_1	R
	1204	sec1_1_1	F
45	1205	sec1_1_1	R
	1206	seg_1_1	F
	1207	seg_1_1	R
	1208	seh_1_1	F
50	1209	seh_1_1	R
	1210	sel_1_1	F
	1211	sel_1_1	R
55	1212	set15_1_1	F
	1213	set15_1_1	R
	1214	set6_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1215	set6_1_1	R
	1216	set7_1_1	F
	1217	set7_1_1	R
	1218	set8_1_1	F
10	1219	set8_1_1	R
	1220	sprV8_1_1	F
	1221	sprV8_1_1	R
15	1222	tst_1_1	F
	1223	tst_1_1	R
	1224	I-sdrC_1_1	F
	1225	I-sdrC_1_1	R
20	1226	I-sdrD_1_1	F
	1227	I-sdrD_1_1	R
	1228	I-sdrE_1_1	F
25	1229	I-sdrE_1_1	R
	1230	b1169_1_1	F
	1231	b1169_1_1	R
	1232	envZ_1_1	F
30	1233	envZ_1_1	R
	1234	fliCb_1_1	F
	1235	fliCb_1_1	R
35	1236	nfrB_1_1	F
	1237	nfrB_1_1	R
	1238	nlpA_1_1	F
	1239	nlpA_1_1	R
40	1240	pilAe_1_1	F
	1241	pilAe_1_1	R
	1242	yacH_1_1	F
45	1243	yacH_1_1	R
	1244	yagX_1_1	F
	1245	yagX_1_1	R
	1246	ycdS_1_1	F
50	1247	ycdS_1_1	R
	1248	yciQ_1_1	F
	1249	yciQ_1_1	R
55	1250	ymcA_1_1	F
	1251	ymcA_1_1	R
	1252	b1202_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1253	b1202_1_1	R
	1254	eae_1_1	F
	1255	eae_1_1	R
	1256	eltB_1_1	F
10	1257	eltB_1_1	R
	1258	escR_1_1	F
	1259	escR_1_1	R
15	1260	escT_1_1	F
	1261	escT_1_1	R
	1262	escU_1_1	F
	1263	escU_1_1	R
20	1264	espB_1_1	F
	1265	espB_1_1	R
	1266	fes_1_1	F
25	1267	fes_1_1	R
	1268	fes_2_1	F
	1269	fes_2_1	R
	1270	fteA_1_1	F
30	1271	fteA_1_1	R
	1272	hlyA_1_1	F
	1273	hlyA_1_1	R
35	1274	hlyB_1_1	F
	1275	hlyB_1_1	R
	1276	iucA_1_1	F
	1277	iucA_1_1	R
40	1278	iucB_1_1	F
	1279	iucB_1_1	R
	1280	iucC_1_1	F
45	1281	iucC_1_1	R
	1282	papG_1_1	F
	1283	papG_1_1	R
	1284	rfbE_1_1	F
50	1285	rfbE_1_1	R
	1286	shuA_1_1	F
55	1287	shuA_1_1	R
	1288	SLTII_1_1	F
	1289	SLTII_1_1	R
	1290	toxA-LTPA_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1291	toxA-LTPA_1_1	R
	1292	VT2vaB_1_1	F
	1293	VT2vaB_1_1	R
	1294	ardeSE0106_1_1	F
10	1295	ardeSE0106_1_1	R
	1296	ardeSE0107_1_1	F
	1297	ardeSE0107_1_1	R
15	1298	aroiSE0105_1_1	F
	1299	aroiSE0105_1_1	R
	1300	atIE_1_1	F
	1301	atIE_1_1	R
20	1302	agrB_1_1	F
	1303	agrB_1_1	R
	1304	agrC_1_1	F
25	1305	agrC_1_1	R
	1306	alphSE1368_1_1	F
	1307	alphSE1368_1_1	R
	1308	gad_1_1	F
30	1309	gad_1_1	R
	1310	glucSE1191_1_1	F
	1311	glucSE1191_1_1	R
35	1312	hsp10_1_1	F
	1313	hsp10_1_1	R
	1314	icaA_1_1	F
	1315	icaA_1_1	R
40	1316	icaB_1_1	F
	1317	icaB_1_1	R
	1318	mvaSSepid_1_1	F
45	1319	mvaSSepid_1_1	R
	1320	nitreSE1972_1_1	F
	1321	nitreSE1972_1_1	R
	1322	nitreSE1974_1_1	F
50	1323	nitreSE1974_1_1	R
	1324	nitreSE1975_1_1	F
	1325	nitreSE1975_1_1	R
55	1326	oiamtSE1209_1_1	F
	1327	oiamtSE1209_1_1	R
	1328	ORF1Sepid_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1329	ORF1Sepid_1_1	R
	1330	ORF3bSepid_1_1	F
	1331	ORF3bSepid_1_1	R
	1332	qacR_1_1	F
10	1333	qacR_1_1	R
	1334	sin_1_1	F
	1335	sin_1_1	R
15	1336	ureSE1861_1_1	F
	1337	ureSE1861_1_1	R
	1338	ureSE1863_1_1	F
	1339	ureSE1863_1_1	R
20	1340	ureSE1864_1_1	F
	1341	ureSE1864_1_1	R
	1342	ureSE1865_1_1	F
25	1343	ureSE1865_1_1	R
	1344	ureSE1867_1_1	F
	1345	ureSE1867_1_1	R
	1346	9caD_1_1	F
30	1347	gcaD_1_1	R
	1348	hld_orf5_1_1	F
	1349	hld_orf5_1_1	R
35	1350	icaC_1_1	F
	1351	icaC_1_1	R
	1352	icaD_1_1	F
	1353	icaD_1_1	R
40	1354	icaR_1_1	F
	1355	icaR_1_1	R
	1356	psm_beta 1 and2_1_1	F
45	1357	psm_beta1and2_1_1	R
	1358	purR_1_1	F
	1359	purR_1_1	R
	1360	spoVG_1_1	F
50	1361	spoVG_1_1	R
	1362	yabJ_1_1	F
55	1363	yabJ_1_1	R
	1364	folQShaemolyt_1_1	F
	1365	folQShaemolyC_1_1	R
	1366	mvaCShaem olyticus_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1367	mvaCShaem olyticus_1 _1	R
	1368	mvaDShaemolyt_1_1	F
	1369	mvaDShaemolyt_1_1	R
	1370	mvaK1Shaemolyticus_1_1	F
10	1371	mvaKiShaemolyticus_1_1	R
	1372	mvaSShaemolyticus_1_1	F
	1373	mvaSShaemolyticus_1_1	R
15	1374	RNApolsigm_1_1	F
	1375	RNApolsigm_1_1	R
	1376	lipShaemolyC1_1	F
	1377	lipShaemolyt_1_1	R
20	1378	agrB2Stalugd_1_1	F
	1379	agrB2Stalugd_1_1	R
	1380	agrC2Stalugd_1_1	F
25	1381	agrC2Stalugd_1_1	R
	1382	agrCStalugd_1_1	F
	1383	agrCStalugd_1_1	R
	1384	slamStalugd_1_1	F
30	1385	slamStalugd_1_1	R
	1386	fblStalugd_1_1	F
	1387	fblStalugd_1_1	R
35	1388	slushABCStalugd_1_1	F
	1389	slushABCStalugd_1_1	R
	1390	RNApolsigmSsapro_1_1	F
	1391	RNApolsigmSsapro_1_1	R
40	1392	RNApolsigmSsapro_1_2	F
	1393	RNApolsigmSsapro_1_2	R
	1394	msrw1Stwar_1_1	F
45	1395	msrw1Stwar_1_1	R
	1396	nukMStwar_1_1	F
	1397	nukMStwar_1_1	R
	1398	proDStwar_1_1	F
50	1399	proDStwar_1_1	R
	1400	proMStwar_1_1	F
	1401	proMStwar_1_1	R
55	1402	sigrpoStwar_1_1	F
	1403	sigrpoStwar_1_1	R
	1404	tnpStwar_1 _1	F

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	SEQ ID NO	Probe name	Direction
5	1405	tnpStwar_1 _1	R
3	1406	gehAStwar_1 _1	F
	1407	gehAStwar_1_1	R
	1408	ARG56_1_1	F
10	1409	ARG56_1_1	R
	1410	ASL43f_1_1	F
	1411	ASL43f_1_1	R
15	1412	BGL2_1_1	F
	1413	BGL2_1_1	R
	1414	CACHS3_1_1	F
	1415	CACHS3_1_1	R
20	1 41 6	CCT8_1_1	F
	1417	CCT8_1_1	R
	1418	CDC37_1_1	F
25	1419	CDC37_1_1	R
	1420	CEF3_1_1	F
	1421	CEF3_1_1	R
	1422	CHS1_1_1	F
30	1423	CHS1_1_1	R
	1424	CHS2_1_1	F
	1425	CHS2_1_1	R
35	1426	CHS4_1_1	F
	1427	CHS4_1_1	R
	1428	CHS5_1_1	F
	1429	CHS5_1_1	R
40	1430	CHT1_1_1	F
	1431	CHT1_1_1	R
	1432	CHT2_1_1	F
45	1433	CHT2_1_1	R
	1434	CHT4_1_1	F
	1435	CHT4_1_1	R
	1436	CSA1_1_1	F
50	1437	CSA1_1_1	R
	1438	5triphosphatase_1 _1	F
	1439	5triphosphatase_1 _1	R
55	1440	AAF1_1_1	F
	1441	AAF1_1_1	R
	1442	ADH1_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1443	ADH1_1_1	R
	1444	ALS1_1_1	F
	1445	ALS1_1_1	R
	1446	ALS7_1_1	F
10	1447	ALS7_1_1	R
	1448	EDT1_1_1	F
	1449	EDT1_1_1	R
15	1450	ELF_1_1	F
	1451	ELF_1_1	R
	1452	ESS1_1_1	F
	1453	ESS1_1_1	R
20	1454	FAL1_1_1	F
	1455	FAL1_1_1	R
	1456	GAP1_1_1	F
25	1457	GAP1_1_1	R
	1458	GNA1_1_1	F
	1459	GNA1_1_1	R
	1460	GSC1_1_1	F
30	1461	GSC1_1_1	R
	1462	GSL1_1_1	F
	1463	GSL1_1_1	R
35	1464	HIS1_1_1	F
	1465	HIS1_1_1	R
	1466	HTS1_1_1	F
	1467	HTS1_1_1	R
40	1468	HWP1_2_1	F
	1469	HWP1_2_1	R
	1470	HYR1_1_1	F
45	1471	HYR1_1_1	R
	1472	INT1a_1_1	F
	1473	INT1a_1_1	R
	1474	KRE15f_1_1	F
50	1475	KRE15f_1_1	R
	1476	KRE6_1_1	F
	1477	KRE6_1_1	R
55	1478	KRE9_1_1	F
	1479	KRE9_1_1	R
	1480	MIG1_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1481	MIG1_1_1	R
	1482	MLS1_1_1	F
	1483	MLS1_1_1	R
	1484	MP65_1_1	F
10	1485	MP65_1_1	R
	1486	NDE1_1_1	F
	1487	NDE1_1_1	R
15	1488	PFK2_1_1	F
	1489	PFK2_1_1	R
	1490	PHR1_1_1	F
	1491	PHR1_1_1	R
20	1492	PHR2_1_1	F
	1493	PHR2_1_1	R
	1494	PHR3_1_1	F
25	1495	PHR3_1_1	R
	1496	PRA1_1_1	F
	1497	PRA1_1_1	R
	1498	PRS1_1_1	F
30	1499	PRS1_1_1	R
	1500	RBT1_1_1	F
	1501	RBT1_1_1	R
35	1502	RBT4_1_1	F
	1503	RBT4_1_1	R
	1504	RHO1_1_1	F
	1505	RHO1_1_1	R
40	1506	RNR1_1_1	F
	1507	RNR1_1_1	R
	1508	RPB7_1_1	F
45	1509	RPB7_1_1	R
	1510	RPL13_1_1	F
	1511	RPL13_1_1	R
	1512	RVS167_1_1	F
50	1513	RVS167_1_1	R
	1514	SHA3_1_1	F
	1515	SHA3_1_1	R
55	1516	SKN1_1_1	F
	1517	SKN1_1_1	R
	1518	SRB1_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1519	SRB1_1_1	R
	1520	TCA1_1_1	F
	1521	TCA1_1_1	R
	1522	TRP1_1_1	F
10	1523	TRP1_1_1	R
	1524	YAE1_1_1	F
	1525	YAE1_1_1	R
15	1526	YRB1_1_1	F
7.5	1527	YRB1_1_1	R
	1528	YST1exon2_1_1	F
	1529	YST1exon2_1_1	R
20	1530	CCN1_1_1	F
	1531	CCN1_1_1	R
	1532	CDC28_1_1	F
25	1533	CDC28_1_1	R
23	1534	CLN2_1_1	F
	1535	CLN2_1_1	R
	1536	CPH1_1_1	F
30	1537	CPH1_1_1	R
	1538	CYB1_1_1	F
	1539	CYB1_1_1	R
35	1540	EFG1_1_1	F
	1541	EFG1_1_1	R
	1542	MNT1_1_1	F
	1543	MNT1_1_1	R
40	1544	RBF1_1_1	F
	1545	RBF1_1_1	R
	1546	RBF1_2_1	F
45	1547	RBF1_2_1	R
	1548	RIM101_1_1	F
	1549	RIM101_1_1	R
	1550	RIM8_1_1	F
50	1551	RIM8_1_1	R
	1552	SEC14_1_1	F
	1553	SEC14_1_1	R
55	1554	SEC4_1_1	F
	1555	SEC4_1_1	R
	1556	TUP1_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1557	TUP1_1_1	R
3	1558	YPT1_1_1	F
	1559	YPT1_1_1	R
	1560	ZNF1CZF1_2_1	F
10	1561	ZNF1CZF1_2_1	R
	1562	arcA_1_1	F
	1563	arcA_1_1	R
15	1564	arcC_1_1	F
	1565	arcC_1_1	R
	1566	bkdA_1_1	F
	1567	bkdA_1_1	R
20	1568	cad_1_1	F
	1569	cad_1_1	R
	1570	camE1_1_1	F
25	1571	camE1_1_1	R
	1572	csrA_1_1	F
	1573	csrA_1_1	R
	1574	dacA_1_1	F
30	1575	dacA_1_1	R
	1576	dfr_1_1	F
	1577	dfr_1_1	R
35	1578	dhoD1a_1_1	F
	1579	dhoD1a_1_1	R
	1580	ABC-eltA_1_1	F
	1581	ABC-eltA_1_1	R
40	1582	agrBfs_1_1	F
	1583	agrBfs_1_1	R
	1584	agrCfs_1_1	F
45	1585	agrCfs_1_1	R
	1586	dnaE_1_1	F
	1587	dnaE_1_1	R
	1588	ebsA_1_1	F
50	1589	ebsA_1_1	R
	1590	ebsB_1_1	F
	1591	ebsB_1_1	R
55	1592	eep_1_1	F
	1593	eep_1_1	R
	1594	efaR_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1595	efaR_1_1	R
	1596	gls24_glsB_1_1	F
	1597	gls24_glsB_1_1	R
	1598	gph_1_1	F
10	1599	gph_1_1	R
	1600	gyrAEf_1 _1	F
	1601	gyrAEf_1 _1	R
15	1602	metEf_1_1	F
	1603	metEf_1_1	R
	1604	mntHCb2_1_1	F
	1605	mntHCb2_1_1	R
20	1606	mob2_1_1	F
	1607	mob2_1_1	R
	1608	mvaD_1_1	F
25	1609	mvaD_1_1	R
20	1610	mvaE_1_1	F
	1611	mvaE_1_1	R
	1612	parC_1 _1	F
30	1613	parC_1 _1	R
	1614	pcfG_1_1	F
	1615	pcfG_1 _1	R
35	1616	phoZ_1_1	F
	1617	phoZ_1_1	R
	1618	polC_1_1	F
	1619	polC_1_1	R
40	1620	ptb_1_1	F
	1621	ptb_1_1	R
	1622	recS1_1_1	F
45	1623	recS1_1_1	R
	1624	rpoN_1_1	F
	1625	rpoN_1_1	R
	1626	tms_1_1	F
50	1627	tms_1_1	R
	1628	tyrDC_1_1	F
	1629	tyrDC_1 _1	R
55	1630	tyrS_1_1	F
	1631	tyrS_1_1	R
	1632	asa1_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1633	asa1_1_1	R
ŭ	1634	asp1_1_1	F
	1635	asp1_1_1	R
	1636	cgh_1_1	F
10	1637	cgh_1_1	R
	1638	cylA_1_1	F
	1639	cylA_1_1	R
15	1640	cylB_1_1	F
	1641	cylB_1_1	R
	1642	cyll_1_1	F
	1643	cyll_1_1	R
20	1644	cylL_cylS_1_1	F
	1645	cylL_cylS_1_1	R
	1646	cylM_1_1	F
25	1647	cylM_1_1	R
	1648	ace_1_1	F
	1649	ace_1_1	R
	1650	ef00108_1_1	F
30	1651	ef00108_1_1	R
	1652	ef00109_1_1	F
	1653	ef00109_1_1	R
35	1654	ef0011_1_1	F
	1655	ef0011_1_1	R
	1656	ef00113_1_1	F
	1657	ef00113_1_1	R
40	1658	ef0012_1_1	F
	1659	ef0012_1_1	R
	1660	ef0022_1_1	F
45	1661	ef0022_1_1	R
	1662	ef0031_1_1	F
	1663	ef0031_1_1	R
	1664	ef0032_1_1	F
50	1665	ef0032_1_1	R
	1666	ef0040_1_1	F
	1667	ef0040_1_1	R
55	1668	ef0058_1_1	F
	1669	ef0058_1_1	R
	1670	enIA_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1671	enIA_1_1	R
3	1672	esa_1_1	F
	1673	esa_1_1	R
	1674	esp_1_1	F
10	1675	esp_1_1	R
	1676	gelE_1_1	F
	1677	gelE_1_1	R
15	1678	groEL_1_1	F
	1679	groEL_1_1	R
	1680	groES_1_1	F
	1681	groES_1_1	R
20	1682	rt1_1_1	F
	1683	rt1_1_1	R
	1684	sala_1_1	F
25	1685	sala_1_1	R
	1686	salb_1_1	F
	1687	salb_1_1	R
	1688	sea1_1_1	F
30	1689	sea1_1_1	R
	1690	sep1_1_1	F
	1691	sep1_1_1	R
35	1692	vicK_1_1	F
	1693	vicK_1_1	R
	1694	yycH_1_1	F
	1695	yycH_1_1	R
40	1696	yycl_1_1	F
	1697	yycl_1_1	R
	1698	yycJ_1_1	F
45	1699	yycJ_1_1	R
	1700	bglB_1_1	F
	1701	bglB_1_1	R
	1702	bglR_1_1	F
50	1703	bglR_1_1	R
	1704	bglS_1_1	F
	1705	bglS_1_1	R
55	1706	efmA_1_1	F
	1707	efmA_1_1	R
	1708	efmb_1_1	F

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	709	efmB_1_1	R
5 17	710	efmC_1_1	F
17	711	efmC_1_1	R
17	712	mreC_1_1	F
10 17	713	mreC_1_1	R
17	714	mreD_1_1	F
17	715	mreD_1_1	R
15	716	mvaDEfaecium_1_1	F
l l	717	mvaDEfaecium_1_1	R
17	718	mvaEEfaecium_1_1	F
17	719	mvaEEfaecium_1_1	R
20 17	720	mvaK1Efaecium_1_1	F
17	721	mvaK1Efaecium_1_1	R
17	722	mvaK2Efaecium_1_1	F
25	723	mvaK2Efaecium_1_1	R
	724	mvaSEfaecium_1_1	F
17	725	mvaSEfaecium_1_1	R
17	726	orf3_4Efaeciumb_1_1	F
30 17	727	orf3_4Efaeciumb_1_1	R
17	728	orf6_7Efaecium_1_1	F
17	729	orf6_7Efaecium_1_1	R
<i>35</i>	730	orf7_8Efaecium_1_1	F
17	731	orf7_8Efaecium_1_1	R
17	732	orf9_10Efaecium_1_1	F
	733	orf9_10Efaecium_1_1	R
17	734	entA_entl_1_1	F
17	735	entA_entl_1_1	R
17	736	entD_1_1	F
45	737	entD_1_1	R
17	738	entR_1_1	F
17	739	entR_1_1	R
	740	oep_1_1	F
17	741	oep_1_1	R
17	742	sagA_1_2	F
17	743	sagA_1_2	R
55	744	atsA_1_1	F
17	745	atsA_1_1	R
17	746	atsB_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1747	atsB_1_1	R
	1748	budC_1_1	F
	1749	budC_1_1	R
	1750	citA_1_1	F
10	1751	citA_1_1	R
	1752	citW_1_1	F
	1753	citW_1_1	R
15	1754	citX_1_1	F
	1755	citX_1_1	R
	1756	dalD_1_1	F
	1757	dalD_1_1	R
20	1758	dalK_1_1	F
	1759	dalK_1_1	R
	1760	dalT_1_1	F
25	1761	dalT_1_1	R
	1762	acoA_1_1	F
	1763	acoA_1_1	R
	1764	acoB_1_1	F
30	1765	acoB_1_1	R
	1766	acoC_1_1	F
	1767	acoC_1_1	R
35	1768	ahlK_1_1	F
	1769	ahlK_1_1	R
	1770	fimK_1_1	F
	1771	fimK_1_1	R
40	1772	glfKPN2_1_1	F
	1773	glfKPN2_1_1	R
	1774	ltrA_1_1	F
45	1775	ltrA_1_1	R
	1776	mdcC_1_1	F
	1777	mdcC_1_1	R
	1778	mdcF_1_1	F
50	1779	mdcF_1_1	R
	1780	mdcH_1_1	F
	1781	mdcH_1_1	R
55	1782	mrkA_1_1	F
	1783	mrkA_1_1	R
	1784	mtrK_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1785	mtrK_1_1	R
	1786	nifF_1_1	F
	1787	nifF_1_1	R
	1788	nifK_1_1	F
10	1789	nifK_1_1	R
	1790	nifN_1_1	F
	1791	nifN_1_1	R
15	1792	tyrP_1_1	F
	1793	tyrP_1_1	R
	1794	ureA_1_1	F
	1795	ureA_1_1	R
20	1796	wbbO_1_1	F
	1797	wbbO_1_1	R
	1798	wza_1_1	F
25	1799	wza_1_1	R
	1800	wzb_1_1	F
	1801	wzb_1_1	R
	1802	wzmKPN2_1_1	F
30	1803	wzmKPN2_1_1	R
	1804	wztKPN2_1_1	F
	1805	wztKPN2_1_1	R
35	1806	yojH_1_1	F
	1807	yojH_1_1	R
	1808	liac_1_1	F
	1809	liac_1_1	R
40	1810 0	cim_1_1	F
	1811	cim_1_1	R
	1812	aldA_1_1	F
45	1813	aldA_1_1	R
	1814	aldA_2_1	F
	1815	aldA_2_1	R
	1816	hemly_1_1	F
50	1817	hemly_1_1	R
	1818	pSL017_1_1	F
	1819	pSL017_1_1	R
55	1820	pSL020_1_1	F
	1821	pSL020_1_1	R
	1822	rcsA_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1823	rcsA_1_1	R
3	1824	rmIC_1_1	F
	1825	rmIC_1_1	R
	1826	rmID_1_1	F
10	1827	rmID_1_1	R
	1828	waaG_1_1	F
	1829	waaG_1_1	R
15	1830	wbbD_1_1	F
10	1831	wbbD_1_1	R
	1832	wbbM_1_1	F
	1833	wbbM_1_1	R
20	1834	wbbN_1_1	F
	1835	wbbN_1_1	R
	1836	wbdA_1_1	F
25	1837	wbdA_1_1	R
	1838	wbdC_1_1	F
	1839	wbdC_1_1	R
	1840	wztKpn_1_1	F
30	1841	wztKpn_1_1	R
	1842	yibD_1_1	F
	1843	yibD_1_1	R
35	1844	cymA_1_1	F
	1845	cymA_1_1	R
	1846	cymD_1_1	F
	1847	cymD_1_1	R
40	1848	cymE_1_1	F
	1849	cymE_1_1	R
	1850	cymH_1_1	F
45	1851	cymH_1_1	R
	1852	cyml_1_1	F
	1853	cyml_1_1	R
	1854	cymJ_1_1	F
50	1855	cymJ_1_1	R
	1856	ddrA_1_1	F
	1857	ddrA_1_1	R
55	1858	fdt-1_1_1	F
	1859	fdt-1_1_1	R
	1860	fdt-2_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1861	fdt-2_1_1	R
	1862	fdt-3_1_1	F
	1863	fdt-3_1_1	R
	1864	gatY_1_1	F
10	1865	gatY_1_1	R
	1866	hydH_1_1	F
	1867	hydH_1_1	R
15	1868	masA_1_1	F
	1869	masA_1_1	R
	1870	nasA_1_1	F
	1871	nasA_1_1	R
20	1872	nasE_1_1	F
	1873	nasE_1_1	R
	1874	nasF_1_1	F
25	1875	nasF_1_1	R
	1876	pehX_1_1	F
	1877	pehX_1_1	R
	1878	pelX_1_1	F
30	1879	pelX_1_1	R
	1880	tagH_1_1	F
	1881	tagH_1 _1	R
35	1882	tagK_1_1	F
	1883	tagK_1_1	R
	1884	tagT_1_1	F
	1885	tagT_1_1	R
40	1886	glpR_1 _1	F
	1887	glpR_1 _1	R
	1888	lasRb_1_1	F
45	1889	lasRb_1_1	R
	1890	OrfX_1_1	F
	1891	OrfX_1_1	R
	1892	pa0260_1_1	F
50	1893	pa0260_1_1	R
	1894	pa0572_1_1	F
	1895	pa0572_1_1	R
55	1896	pa0625_1_1	F
	1897	pa0625_1_1	R
	1898	pa0636_1_1	F

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	SEQ ID NO	Probe name	Direction
5	1899	pa0636_1_1	R
	1900	pa1046_1_1	F
	1901	pa1046_1_1	R
	1902	pa1069_1_1	F
10	1903	pa1069_1_1	R
	1904	pa1846_1_1	F
	1905	pa1846_1_1	R
15	1906	pa3866_1_1	F
	1907	pa3866_1_1	R
	1908	pa4082_1_1	F
	1909	pa4082_1_1	R
20	1910	pilAp_1_1	F
	1911	pilAp_1_1	R
	1912	PilAp2_1_1	F
25	1913	PilAp2_1_1	R
	1914	pilC_1_1	F
	1915	pilC_1_1	R
	1916	PstP_1_1	F
30	1917	PstP_1_1	R
	1918	purK_1_1	F
	1919	purK_1_1	R
35	1920	uvrDII_1_1	F
	1921	uvrDII_1_1	R
	1922	vsml_1_1	F
	1923	vsml_1_1	R
40	1924	vsmR_1_2	F
	1925	vsmR_1_2	R
	1926	xcpX_1_1	F
45	1927	xcpX_1_1	R
	1928	aprA_1_1	F
	1929	aprA_1_1	R
	1930	aprE_1_1	F
50	1931	aprE_1_1	R
	1932	ctx_1_2	F
	1933	ctx_1_2	R
55	1934	algB_1_1	F
	1935	algB_1_1	R
	1936	algN_1_1	F
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	SEQ ID NO	Probe name	Direction
5	1937	algN_1_1	R
3	1938	algR_1_1	F
	1939	algR_1_1	R
	1940	ExoS_1_1	F
10	1941	ExoS_1_1	R
	1942	fpvA_1_1	F
	1943	fpvA_1_1	R
15	1944	lasRa_1_1	F
	1945	lasRa_1_1	R
	1946	lipA_1_1	F
	1947	lipA_1_1	R
20	1948	lipH_1_1	F
	1949	lipH_1_1	R
	1950	Orf159_1_2	F
25	1951	Orf159_1_2	R
	1952	Orf252_1_1	F
	1953	Orf252_1_1	R
	1954	pchG_1_1	F
30	1955	pchG_1_1	R
	1956	PhzA_1_1	F
	1957	PhzA_1_1	R
35	1958	PhzB_1_1	F
	1959	PhzB_1_1	R
	1960	PLC_1_1	F
	1961	PLC_1_1	R
40	1962	plcN_1_1	F
	1963	plcN_1_1	R
	1964	plcR_1_1	F
45	1965	plcR_1 _1	R
	1966	pvdD_1_1	F
	1967	pvdD_1_1	R
	1968	pvdF_1_2	F
50	1969	pvdF_1_2	R
	1970	pyocinS1_1_1	F
	1971	pyocinS1_1_1	R
55	1972	pyocinS1im_1_1	F
	1973	pyocinS1im_1_1	R
	1974	pyocinS2_1 _1	F

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	SEQ ID NO	Probe name	Direction
5	1975	pyocinS2_1 _1	R
	1976	pys2_1_1	F
	1977	pys2_1_1	R
	1978	pys2_2_1	F
10	1979	pys2_2_1	R
	1980	rbf303_1_1	F
	1981	rbf303_1_1	R
15	1982	rhlA_1_1	F
	1983	rhlA_1_1	R
	1984	rhlB_1_1	F
	1985	rhlB_1_1	R
20	1986	rhIR_1_1	F
	1987	rhIR_1_1	R
	1988	TnAP41_1_2	F
25	1989	TnAP41_1_2	R
	1990	toxA_1_1	F
	1991	toxA_1_1	R
	1992	cap1 EStrpneu_1_1	F
30	1993	cap1 EStrpneu_1_1	R
	1994	cap1 FStrpneu_1_1	F
	1995	cap1 FStrpneu_1_1	R
35	1996	cap1 GStrpneu_1_1	F
	1997	cap1 GStrpneu_1_1	R
	1998	cap3AStrpneu_1_1	F
	1999	cap3AStrpneu_1 _1	R
40	2000	cap3BStrpneu_1_1	F
	2001	cap3BStrpneu_1_1	R
	2002	celAStrpneu_1_1	F
45	2003	celAStrpneu_1_1	R
	2004	celBStrpneu_1_1	F
	2005	celBStrpneu_1_1	R
	2006	cglAStrpneu_1_1	F
50	2007	cglAStrpneu_1_1	R
	2008	cglBStrpneu_1_1	F
	2009	cglBStrpneu_1_1	R
55	2010	cglCStrpneu_1_1	F
	2011	cglCStrpneu_1_1	R
	2012	cgIDStrpneu_1_1	F

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	SEQ ID NO	Probe name	Direction
5	2013	cgIDStrpneu_1_1	R
	2014	cinA_1_1	F
	2015	cinA_1_1	R
	2016	cps14EStrpneum_1_1	F
10	2017	cps14EStrpneum_1_1	R
	2018	cps14FStrpneum_1_1	F
	2019	cps14FStrpneum_1_1	R
15	2020	cps14GStrpneum_1_1	F
	2021	cps14GStrpneum_1_1	R
	2022	cps14HStrpneum_1_1	F
	2023	cps14HStrpneum_1_1	R
20	2024	cps19aHStrpneum_1_1	F
	2025	cps19aHStrpneum_1_1	R
	2026	cps19alStrpneum_1_1	F
25	2027	cps19alStrpneum_1_1	R
	2028	cps19aKStrpneum_1_1	F
	2029	cps19aKStrpneum_1_1	R
	2030	cps19fGStrpneum_1_1	F
30	2031	cps19fGStrpneum_1_1	R
	2032	cps23fGStrpneum_1_1	F
	2033	cps23fGStrpneum_1_1	R
35	2034	dexB_1_1	F
	2035	dexB_1_1	R
	2036	dinF_1_1	F
	2037	dinF_1_1	R
40	2038	1760Strpneu_1_1	F
	2039	1760Strpneu_1_1	R
	2040	acyPStrpneu_1_1	F
45	2041	acyPStrpneu_1_1	R
	2042	endAStrpneu_1_1	F
	2043	endAStrpneu_1_1	R
	2044	exoAStrpneu_1_1	F
50	2045	exoAStrpneu_1_1	R
	2046	exp72_1_1	F
	2047	exp72_1_1	R
55	2048	fnlAStrpneu_1_1	F
	2049	fnlAStrpneu_1_1	R
	2050	fnlBStrpneu_1_1	F
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	SEQ ID NO	Probe name	Direction
5	2051	fnlBStrpneu_1_1	R
3	2052	fnlCStrpneu_1_1	F
	2053	fnlCStrpneu_1_1	R
	2054	gct18Strpneum_1_1	F
10	2055	gct18Strpneum_1_1	R
	2056	hexB1_1_1	F
	2057	hexB1_1_1	R
15	2058	hftsHstrpneu_1 _1	F
10	2059	hftsHstrpneu_1_1	R
	2060	immunofrag1Strpneu_1_1	F
	2061	immunofrag1Strpneu_1_1	R
20	2062	immunofrag2Strpneu_2_1	F
	2063	immunofrag2Strpneu_2_1	R
	2064	immunofrag3Strpneu_2_1	F
25	2065	immunofrag3Strpneu_2_1	R
	2066	kdtBStrpneu_1_1	F
	2067	kdtBStrpneu_1_1	R
	2068	lysAStrpneu_1_1	F
30	2069	lysAStrpneu_1_1	R
	2070	pcpBStrpneu_1_1	F
	2071	pcpBStrpneu_1 _1	R
35	2072	pflCStrpneu_1_1	F
	2073	pflCStrpneu_1_1	R
	2074	plpA_1_1	F
	2075	plpA_1_1	R
40	2076	prtA1 Strpneu_1_1	F
	2077	prtA1 Strpneu_1_1	R
	2078	pspC1Strpneu_1_1	F
45	2079	pspC1Strpneu_1_1	R
	2080	pspC2_1_1	F
	2081	pspC2_1_1	R
	2082	purRStrpneu_1_1	F
50	2083	purRStrpneu_1_1	R
	2084	pyrDAStrpneum_1_1	F
	2085	pyrDAStrpneum_1_1	R
55	2086	SP0828Strpneu_1_1	F
	2087	SP0828Strpneu_1_1	R
	2088	SP0830Strpneu_1_1	F

	SEQ ID NO	Probe name	Direction
5	2089	SP0830Strpneu_1_1	R
3	2090	SP0833Strpneu_1_1	F
	2091	SP0833Strpneu_1 _1	R
	2092	SP0837_38Strpneu_1_1	F
10	2093	SP0837_38Strpneu_1 _1	R
	2094	SP0839Strpneu_1 _1	F
	2095	SP0839Strpneu_1 _1	R
15	2096	ugdStrpneu_1_1	F
7.5	2097	ugdStrpneu_1_1	R
	2098	uncC_1_1	F
	2099	uncC_1_1	R
20	2100	vicXStrepneu_1_1	F
	2101	vicXStrepneu_1 _1	R
	2102	wchA6bStrpneum_1 _1	F
25	2103	wchA6bStrpneum_1 _1	R
	2104	wci4Strpneum_1_1	F
	2105	wci4Strpneum_1_1	R
	2106	wciK4Strpneum_1_1	F
30	2107	wciK4Strpneum_1_1	R
	2108	wciL4Strpneum_1_1	F
	2109	wciL4Strpneum_1_1	R
35	2110	wciN6bStrpneum_1_1	F
	2111	wciN6bStrpneum_1_1	R
	2112	wciO6bStrpneum_1_1	F
	2113	wciO6bStrpneum_1_1	R
40	2114	wciP6bStrpneum_1_1	F
	2115	wciP6bStrpneum_1_1	R
	2116	wciY18Strpneum_1 _1	F
45	2117	wciY18Strpneum_1_1	R
	2118	wzdbStrpneum_1_1	F
	2119	wzdbStrpneum_1_1	R
	2120	wze6bStrpneum_1_1	F
50	2121	wze6bStrpneum_1_1	R
	2122	wzy18Strpneum_1_1	F
	2123	wzy18Strpneum_1_1	R
55	2124	wzy4Strpneum_1_1	F
	2125	wzy4Strpneum_1_1	R
	2126	wzy6bStrpneum_1_1	F

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	SEQ ID NO	Probe name	Direction
5	2127	wzy6bStrpneum_1_1	R
	2128	xpt_1 _1	F
	2129	xpt_1 _1	R
	2130	igaStrpneu_1 _1	F
10	2131	igaStrpneu_1 _1	R
	2132	lytA_1_1	F
	2133	lytA_1_1	R
15	2134	nanA_1_1	F
	2135	nanA_1_1	R
	2136	nanBStrpneu_1_1	F
	2137	nanBStrpneu_1_1	R
20	2138	pcpCStrpneu_1_1	F
	2139	pcpCStrpneu_1_1	R
	2140	ply_1_1	F
25	2141	ply_1_1	R
	2142	prtAStrpneu_1_1	F
	2143	prtAStrpneu_1_1	R
	2144	pspA_1_2	F
30	2145	pspA_1_2	R
	2146	SP0834Strpneu_1_1	F
	2147	SP0834Strpneu_1_1	R
35	2148	SP0834Strpneu_1_2	F
	2149	SP0834Strpneu_1_2	R
	2150	sphtraStrpneu_1_1	F
	2151	sphtraStrpneu_1_1	R
40	2152	wciJStrpneu_1_1	F
	2153	wciJStrpneu_1_1	R
	2154	wziyStrpneu_1_1	F
45	2155	wziyStrpneu_1_1	R
	2156	wzxStrpneu_1_1	F
	2157	wzxStrpneu_1_1	R
	2158	cpsA1Strgal_1_1	F
50	2159	cpsA1Strgal_1_1	R
	2160	cpsB1Strgal_1_1	F
	2161	cpsB1Strgal_1_1	R
55	2162	cpsC1Strgal_1_1	F
	2163	cpsC1Strgal_1_1	R
	2164	cpsD1Strgal_1_1	F
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	SEQ ID NO	Probe name	Direction
5	2165	cpsD1Strgal_1_1	R
	2166	cpsE1Strgal_1_1	F
	2167	cpsE1Strgal_1_1	R
	2168	cpsG1Strgal_1_1	F
10	2169	cpsG1Strgal_1_1	R
	2170	cpslStragal_1_1	F
	2171	cpslStragal_1_1	R
15	2172	cpsJStragal_1_1	F
	2173	cpsJStragal_1_1	R
	2174	cpsKStragal_1_1	F
	2175	cpsKStragal_1_1	R
20	2176	cpsMStragal_1_1	F
	2177	cpsMStragal_1_1	R
	2178	cpsYStragal_1_1	F
25	2179	cpsYStragal_1 _1	R
	2180	cpsYStragal_2_1	F
	2181	cpsYStragal_2_1	R
	2182	cylBStraga_1_1	F
30	2183	cylBStraga_1_1	R
	2184	cylEStraga_1_1	F
	2185	cylEStraga_1_1	R
35	2186	cylFStraga_1_1	F
	2187	cylFStraga_1_1	R
	2188	cylHStraga_1_1	F
	2189	cylHStraga_1_1	R
40	2190	cyllStraga_1_1	F
	2191	cyllStraga_1_1	R
	2192	cylJStraga_1_1	F
45	2193	cylJStraga_1_1	R
	2194	cylKStraga_1_1	F
	2195	cylKStraga_1_1	R
	2196	0487Straga_1_1	F
50	2197	0487Straga_1_1	R
	2198	0488Straga_1_1	F
	2199	0488Straga_1_1	R
55	2200	0493Straga_1_1	F
	2201	0493Straga_1_1	R
	2202	0495Straga_1_1	F

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	SEQ ID NO	Probe name	Direction
5	2203	0495Straga_1_1	R
	2204	0498Straga_1_1	F
	2205	0498Straga_1_1	R
	2206	0500Straga_1_1	F
10	2207	0500Straga_1_1	R
	2208	0502Straga_1_1	F
	2209	0502Straga_1_1	R
15	2210	0504Straga_1_1	F
	2211	0504Straga_1_1	R
	2212	foIDStraga_1_1	F
	2213	foIDStraga_1_1	R
20	2214	neuA1Strgal_1_1	F
	2215	neuA1Strgal_1_1	R
	2216	neuB1Strgal_1_1	F
25	2217	neuB1Strgal_1_1	R
	2218	neuC1Strgal_1_1	F
	2219	neuC1Strgal_1_1	R
	2220	neuD1Strgal_1 _1	F
30	2221	neuD1Strgal_1_1	R
	2222	recNStraga_1_1	F
	2223	recNStraga_1_1	R
35	2224	ileSStraga_1_1	F
	2225	ileSStraga_1_1	R
	2226	CAMPfactor_1_1	F
	2227	CAMPfactor_1_1	R
40	2228	CAMPfactor_2_1	F
	2229	CAMPfactor_2_1	R
	2230	0499Straga_1_1	F
45	2231	0499Straga_1_1	R
	2232	hylStragal_1_1	F
	2233	hylStragal_1_1	R
	2234	lipStragal_1_1	F
50	2235	lipStragal_1_1	R
	2236	cyclStrpyog_1_1	F
	2237	cyclStrpyog_1_1	R
55	2238	fah_rph_hlo_Strpyog_1_1	F
	2239	fah_rph_hlo_Strpyog_1_1	R
	2240	int_1_1	F
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	SEQ ID NO	Probe name	Direction
5	2241	int_1_1	R
	2242	int315.5_1_1	F
	2243	int315.5_1_1	R
	2244	murEStrpyog_1_1	F
10	2245	murEStrpyog_1_1	R
	2246	oppA_1_1	F
	2247	oppA_1_1	R
15	2248	oppCStrpyog_1_1	F
	2249	oppCStrpyog_1_1	R
	2250	oppD_1_1	F
	2251	oppD_1_1	R
20	2252	SPy0382Strpyog_1_1	F
	2253	SPy0382Strpyog_1_1	R
	2254	SPy0390Strpyog_1_1	F
25	2255	SPy0390Strpyog_1_1	R
	2256	SpyM3_1351_1_1	F
	2257	SpyM3_1351_1_1	R
	2258	vicXStrpyog_1_1	F
30	2259	vicXStrpyog_1 _1	R
	2260	DNaselStrpyog_1_1	F
	2261	DNaselStrpyog_1_1	R
35	2262	fba2Strpyog_1_1	F
	2263	fba2Strpyog_1 _1	R
	2264	fhuAStrpyog_1 _1	F
	2265	fhuAStrpyog_1 _1	R
40	2266	fhuB1Strpyog_1_1	F
	2267	fhuB1Strpyog_1_1	R
	2268	fhuDStrpyog_1_1	F
45	2269	fhuDStrpyog_1_1	R
	2270	fhuGStrpyog_1_1	F
	2271	fhuGStrpyog_1_1	R
	2272	hylA_1_1	F
50	2273	hylA_1_1	R
	2274	hylP_1_1	F
	2275	hyIP_1_1	R
55	2276	hylp2_1_1	F
	2277	hylp2_1_1	R
	2278	oppB_1_1	F

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	SEQ ID NO	Probe name	Direction
5	2279	oppB_1_1	R
	2280	ropB_1_1	F
	2281	ropB_1_1	R
	2282	scpAStrpyog_1_1	F
10	2283	scpAStrpyog_1_1	R
	2284	sloStrpyog_1_1	F
	2285	sloStrpyog_1_1	R
15	2286	smez-4Strpyog_1_1	F
	2287	smez-4Strpyog_1_1	R
	2288	sof_1_1	F
	2289	sof_1_1	R
20	2290	sof_2_1	F
	2291	sof_2_1	R
	2292	speA_1_1	F
25	2293	speA_1_1	R
	2294	speB2Strpyog_1_1	F
	2295	speB2Strpyog_1_1	R
	2296	speCStrpyog_1_1	F
30	2297	speCStrpyog_1_1	R
	2298	speJStrpyog_1_1	F
	2299	speJStrpyog_1_1	R
35	2300	srtBStrpyog_1_1	F
	2301	srtBStrpyog_1_1	R
	2302	srtCStrpyog_1_1	F
	2303	srtCStrpyog_1_1	R
40	2304	srtEStrpyog_1_1	F
	2305	srtEStrpyog_1_1	R
	2306	srtFStrpyog_1_1	F
45	2307	srtFStrpyog_1_1	R
	2308	srtGStrpyog_1_1	F
	2309	srtGStrpyog_1_1	R
	2310	srtlStrpyog_1_1	F
50	2311	srtlStrpyog_1_1	R
	2312	srtKStrpyog_1_1	F
	2313	srtKStrpyog_1_1	R
55	2314	srtRStrpyog_1_1	F
	2315	srtRStrpyog_1_1	R
	2316	srtTStrpyog_1_1	F
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	SEQ ID NO	Probe name	Direction
5	2317	srtTStrpyog_1_1	R
3	2318	vicKStrpyog_1_1	F
	2319	vicKStrpyog_1_1	R
	2320	573Stprmut_1_1	F
10	2321	573Stprmut_1_1	R
	2322	580SStprmut_1_1	F
	2323	580SStprmut_1_1	R
15	2324	581_582SStprmut_1_1	F
	2325	581_582SStprmut_1_1	R
	2326	584SStprmut_1_1	F
	2327	584SStprmut_1_1	R
20	2328	dltAStrmut_1_1	F
	2329	dltAStrmut_1_1	R
	2330	dltBStrmut_1_1	F
25	2331	dltBStrmut_1_1	R
	2332	dltCppx1Strmut_1_1	F
	2333	dltCppx1Strmut_1_1	R
	2334	dltDStrmut_1_1	F
30	2335	dltDStrmut_1_1	R
	2336	lichStrbov_1_1	F
	2337	lichStrbov_1_1	R
35	2338	lytRStprmut_1_1	F
	2339	lytRStprmut_1_1	R
	2340	lytSStprmut_1_1	F
	2341	lytSStprmut_1_1	R
40	2342	pepQStrrmut_1_1	F
	2343	pepQStrrmut_1_1	R
	2344	pflCStrmut_1_1	F
45	2345	pflCStrmut_1_1	R
	2346	recNStprmut_1_1	F
	2347	recNStprmut_1_1	R
	2348	ytqBStrm ut_1 _1	F
50	2349	ytqBStrmut_1_1	R
	2350	hlyXStrmut_1_1	F
	2351	hlyXStrmut_1_1	R
55	2352	igaStrmitis_1_1	F
	2353	igaStrmitis_1_1	R
	2354	igaStrsanguis_1_1	F

	SEQ ID NO	Probe name	Direction
5	2355	igaStrsanguis_1_1	R
3	2356	perMStrmut_1_1	F
	2357	perMStrmut_1_1	R
	2358	atfA_1_1	F
10	2359	atfA_1_1	R
	2360	atfB_1_1	F
	2361	atfB_1_1	R
15	2362	atfC_1_1	F
	2363	atfC_1_1	R
	2364	ccmPrmi1_1_1	F
	2365	ccmPrmi1_1_1	R
20	2366	cyaPrmi_1_1	F
	2367	cyaPrmi_1_1	R
	2368	aad_1_1	F
25	2369	aad_1_1	R
	2370	flfB_1_1	F
	2371	flfB_1_1	R
	2372	flfD_1_1	F
30	2373	flfD_1_1	R
	2374	flfN_1_1	F
	2375	flfN_1_1	R
35	2376	flhD_1_1	F
	2377	flhD_1_1	R
	2378	floA_1_1	F
	2379	floA_1_1	R
40	2380	ftsK_1_1	F
	2381	ftsK_1_1	R
	2382	gstB_1_1	F
45	2383	gstB_1_1	R
	2384	hemCPrmi_1_1	F
	2385	hemCPrmi_1_1	R
	2386	hemDPrmi_1_1	F
50	2387	hemDPrmi_1_1	R
	2388	hev_1_1	F
	2389	hev_1_1	R
55	2390	katA_1_1	F
	2391	katA_1_1	R
	2392	lpp1_1_1	F
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	SEQ ID NO	Probe name	Direction
5	2393	lpp1_1_1	R
	2394	menE_1_1	F
	2395	menE_1_1	R
	2396	mfd_1_1	F
10	2397	mfd_1_1	R
	2398	nrpA_1_1	F
	2399	nrpA_1_1	R
15	2400	nrpB_1_1	F
	2401	nrpB_1_1	R
	2402	nrpG_1_1	F
	2403	nrpG_1_1	R
20	2404	nrpS_1_1	F
	2405	nrpS_1_1	R
	2406	nrpT_1_1	F
25	2407	nrpT_1_1	R
	2408	nrpU_1_1	F
	2409	nrpU_1_1	R
	2410	pat_1_1	F
30	2411	pat_1_1	R
	2412	pmfA_1_1	F
	2413	pmfA_1_1	R
35	2414	pmfC_1_1	F
	2415	pmfC_1_1	R
	2416	pmfE_1_1	F
	2417	pmfE_1_1	R
40	2418	ppaA_1_1	F
	2419	ppaA_1_1	R
	2420	rsbA_1_1	F
45	2421	rsbA_1_1	R
	2422	rsbC_1_1	F
	2423	rsbC_1_1	R
	2424	speB_1_1	F
50	2425	speB_1_1	R
	2426	stmA_1_1	F
	2427	stmA_1_1	R
55	2428	stmB_1_1	F
	2429	stmB_1_1	R
	2430	terA_1_1	F

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	SEQ ID NO	Probe name	Direction
5	2431	terA_1_1	R
	2432	terD_1_1	F
	2433	terD_1_1	R
	2434	umoA_1_1	F
10	2435	umoA_1_1	R
	2436	umoB_1_1	F
	2437	umoB_1_1	R
15	2438	umoC_1_1	F
	2439	umoC_1_1	R
	2440	ureR_1_1	F
	2441	ureR_1_1	R
20	2442	xerC_1_1	F
	2443	xerC_1_1	R
	2444	ygbA_1_1	F
25	2445	ygbA_1_1	R
	2446	flaA_1_1	F
	2447	flaA_1_1	R
	2448	flaD_1_1	F
30	2449	flaD_1_1	R
	2450	fliA_1_1	F
	2451	fliA_1_1	R
35	2452	hpmA_1_1	F
	2453	hpmA_1_1	R
	2454	hpmB_1_1	F
	2455	hpmB_1_1	R
40	2456	lpsPrmi_1_1	F
	2457	lpsPrmi_1_1	R
	2458	mrpA_1_1	F
45	2459	mrpA_1_1	R
	2460	mrpB_1_1	F
	2461	mrpB_1_1	R
	2462	mrpC_1_1	F
50	2463	mrpC_1_1	R
	2464	mrpD_1_1	F
	2465	mrpD_1_1	R
55	2466	mrpE_1_1	F
	2467	mrpE_1_1	R
	2468	mrpF_1_1	F
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	SEQ ID NO	Probe name	Direction
5	2469	mrpF_1_1	R
	2470	mrpG_1_1	F
	2471	mrpG_1_1	R
	2472	mrpH_1_1	F
10	2473	mrpH_1_1	R
	2474	mrpl_1_1	F
	2475	mrpl_1_1	R
15	2476	mrpJ_1_1	F
	2477	mrpJ_1_1	R
	2478	patA_1_1	F
	2479	patA_1_1	R
20	2480	putA_1_1	F
	2481	putA_1_1	R
	2482	uca_1_1	F
25	2483	uca_1_1	R
	2484	ureDPrmi_1_1	F
	2485	ureDPrmi_1_1	R
	2486	ureEPrmi_1_1	F
30	2487	ureEPrmi_1_1	R
	2488	ureFPrmi_1_1	F
	2489	ureFPrmi_1_1	R
35	2490	zapA_1_1	F
	2491	zapA_1_1	R
	2492	zapB_1_1	F
	2493	zapB_1_1	R
40	2494	zapD_1_1	F
	2495	zapD_1_1	R
	2496	zapE_1_1	F
45	2497	zapE_1_1	R
	2498	envZPrvu_1_1	F
	2499	envZPrvu_1_1	R
	2500	frdC_1_1	F
50	2501	frdC_1_1	R
	2502	frdD_1_1	F
	2503	frdD_1_1	R
55	2504	infBPrvu_1_1	F
	2505	infBPrvu_1_1	R
	2506	lad_1_1	F

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	2508	tna2_1_1	F
	2509	tna2_1_1	R
	2510	end_1_1	F
10	2511	end_1_1	R
	2512	pqrA_1_1	F
	2513	pqrA_1_1	R
15	2514	urg_1_1	F
	2515	urg_1_1	R
	2516	blalMP-7_1_1	F
	2517	blalMP-7_1_1	R
20	2518	meclSepid_1_1	F
	2519	meclSepid_1_1	R
	2520	blaOXA-10_1_2	F
25	2521	blaOXA-10_1_2	R
	2522	blaB_1_1	F
	2523	blaB_1_1	R
	2524	ampC_1_1	F
30	2525	ampC_1_1	R
	2526	I-blaR_1_1	F
	2527	I-blaR_1_1	R
35	2528	blaOXA- 32_1_1	F
	2529	blaOXA- 32_1_1	R
	2530	bla-CTX-M-22_1 _1	F
	2531	bla-CTX-M-22_1_1	R
40	2532	pbp2aStrpneu_1_1	F
	2533	pbp2aStrpneu_1_1	R
	2534	blaSHV-1_1_1	F
45	2535	blaSHV-1_1_1	R
	2536	blaOXA- 2_1_1	F
	2537	blaOXA-2_1_12_1_1	R
	2538	blaRShaemolyt_1_1	F
50	2539	blaRShaemolyt_1_1	R
	2540	blaIMP-7_1_2	F
	2541	blaIMP-7_1_2	R
55	2542	I-mecR_1_1	F
	2543	I-mecR_1_1	R
	2544	blaOXY_1_1	F

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	SEQ ID NO	Probe name	Direction
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	2546	dacCStrpyog_1_1	F
	2547	dacCStrpyog_1_1	R
	2548	femA_1_1	F
10	2549	femA_1_1	R
	2550	mecA_1_1	F
	2551	mecA_1_1	R
15	2552	blalShaemolyt_1_1	F
	2553	blalShaemolyt_1_1	R
	2554	blavim_1_1	F
	2555	blavim_1_1	R
20	2556	pbp2b_1_1	F
	2557	pbp2b_1_1	R
	2558	pbp2primeSepid_1_1	F
25	2559	pbp2primeSepid_1_1	R
	2560	pbp2x_1_1	F
	2561	pbp2x_1_1	R
	2562	pbp3Saureuc_1_1	F
30	2563	pbp3Saureuc_1_1	R
	2564	pbp4_1_1	F
	2565	pbp4_1_1	R
35	2566	pbp5Efaecium_1_1	F
	2567	pbp5Efaecium_1_1	R
	2568	pbpC_1_1	F
	2569	pbpC_1_1	R
40	2570	I-mecl_1_1	F
	2571	I-mecl_1_1	R
	2572	pbp1a_1_1	F
45	2573	pbp1a_1_1	R
	2574	I-blal_1_1	F
	2575	I-blal_1_1	R
	2576	blaTEM-106_1_1	F
50	2577	blaTEM-106_1_1	R
	2578	blaOXY-KLOX_1_1	F
	2579	blaOXY-KLOX_1_1	R
55	2580	ftsWEF_1_1	F
	2581	ftsWEF_1_1	R
	2582	fmhB_1_1	F
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	2584	cumA_1_1	F
	2585	cumA_1_1	R
	2586	femBShaemolyt_1_1	F
10	2587	femBShaemolyt_1_1	R
	2588	blaPER-1_1_1	F
	2589	blaPERI-1_1_1	R
15	2590	bla_FOX-3_1_1	F
	2591	bla_FOX-3_1_1	R
	2592	blaA_1_1	F
	2593	blaA_1_1	R
20	2594	psrb_1_1	F
	2595	Psrb_1_1	R
	2596	fmhA_1_1	F
25	2597	fmhA_1_1	R
	2598	mecR1Sepid_1_1	F
	2599	mecR1Sepid_1_1	R
	2600	blaZ_1_1	F
30	2601	blaZ_1_1	R
	2602	blaOXA-1_1_1	F
	2603	blaOXA-1_1_1	R
35	2604	fox-6_1_1	F
	2605	fox-6_1_1	R
	2606	blaPrmi_1_1	F
	2607	blaPrmi_1_1	R
40	2608	aacA_aph DStwar_1 _1	F
	2609	aacA_aphDStwar_1_1	R
	2610	aacC1_1_2	F
45	2611	aacC1_1_2	R
	2612	aacC2_1_1	F
	2613	aacC2_1_1	R
	2614	strB_1_1	F
50	2615	strB_1_1	R
	2616	aadA_1_1	F
	2617	aadA_1_1	R
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	2619	aadB_1_2	R
	2620	aadD_1_1	F
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	2623	aacA4_1_2	R
	2624	strA_1_1	F
10	2625	strA_1_1	R
	2626	aph-A3_1_1	F
	2627	aph-A3_1_1	R
15	2628	aacC1_1_1	F
	2629	aacC1_1_1	R
	2630	aacA4_1_1	F
	2631	aacA4_1_1	R
20	2632	aacA-aphD_1_1	F
	2633	aacA-aphD_1_1	R
	2634	I-spc_1_1	F
25	2635	I-spc_1_1	R
	2636	aphA3_1_1	F
	2637	aphA3_1_1	R
	2638	ermC_1_1	F
30	2639	ermC_1_1	R
	2640	linB_1_1	F
	2641	linB_1_1	R
35	2642	satSA_1_1	F
	2643	satSA_1_1	R
	2644	mdrSA_1_1	F
	2645	mdrSA_1_1	R
40	2646	I-linA_1_1	F
	2647	I-linA_1_1	R
	2648	ermB_1_2	F
45	2649	ermB_1_2	R
	2650	ermA_1_1	F
	2651	ermA_1_1	R
	2652	satA_1_1	F
50	2653	satA_1_1	R
	2654	msrA_1_1	F
	2655	msrA_1_1	R
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	2657	mphBM_1_1	R
	2658	mefA_1_1	F
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	SEQ ID NO	Probe name	Direction
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	2660	mrx_1_1	F
	2661	mrx_1_1	R
	2662	dfrStrpneu_1_1	F
10	2663	dfrStrpneu_1_1	R
	2664	dfrA_1_1	F
	2665	dfrA_1_1	R
15	2666	cmlA5_1_1	F
10	2667	cmIA5_1_1	R
	2668	catEfaecium_1_1	F
	2669	catEfaecium_1_1	R
20	2670	cat_1_1	F
	2671	cat_1_1	R
	2672	tetAJ_1_1	F
25	2673	tetAJ_1_1	R
	2674	tetL_1_1	F
	2675	tetL_1_1	R
	2676	tetM_1_1	F
30	2677	tetM_1_1	R
	2678	vanH(tn)_1 _1	F
	2679	vanH(tn)_1 _1	R
35	2680	vanA_1_1	F
	2681	vanA_1_1	R
	2682	vanHB2_1_1	F
	2683	vanHB2_1_1	R
40	2684	vanR_1_1	F
	2685	vanR_1_1	R
	2686	vanRB2_1_1	F
45	2687	vanRB2_1_1	R
	2688	vanS(tn)_1_1	F
	2689	vanS(tn)_1_1	R
	2690	vanSB2_1_1	F
50	2691	vanSB2_1_1	R
	2692	vanWB2_1_1	F
	2693	vanWB2_1_1	R
55	2694	ddl_1_1	F
	2695	ddl_1_1	R
	2696	ble_1_1	F

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	SEQ ID NO	Probe name	Direction
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	2699	vanXB2_1_1	R
	2700	vanY(tn)_1_1	F
10	2701	vanY(tn)_1_1	R
	2702	vanYB2_1_1	F
	2703	vanYB2_1_1	R
15	2704	vanB_1_1	F
	2705	vanB_1_1	R
	2706	vanZ(tn)_1_1	F
	2707	vanZ(tn)_1_1	R
20	2708	vanC-2_1_1	F
	2709	vanC-2_1_1	R
	2710	vanX(tn)_1_1	F
25	2711	vanX(tn)_1_1	R
	2712	acrB_1_1	F
	2713	acrB_1_1	R
	2714	mexB_1_2	F
30	2715	mexB_1_2	R
	2716	I-qacA_1 _1	F
	2717	I-qacA_1_1	R
35	2718	sull_1_1	F
	2719	sull_1_1	R
	2720	sul_1_1	F
	2721	sul_1_1	R
40	2722	cadBStalugd_1_1	F
	2723	cadBStalugd_1_1	R
	2724	mexA_1_1	F
45	2725	mexA_1_1	R
	2726	acrR_1_1	F
	2727	acrR_1_1	R
	2728	emeA_1_1	F
50	2729	emeA_1_1	R
	2730	acrA_1_1	F
	2731	acrA_1_1	R
55	2732	rtn_1_1	F
	2733	rtn_1_1	R
	2734	abcXStrpmut_1_1	F

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	2737	qacEdelta1_1_1	R
	2738	elkT-abcA_1_1	F
10	2739	elkT-abcA_1_1	R
	2740	I-cadA_1_1	F
	2741	I-cadA_1_1	R
15	2742	albA_1_1	F
	2743	albA_1_1	R
	2744	wzm_1_1	F
	2745	wzm_1_1	R
20	2746	msrCb_1_1	F
	2747	msrCb_1_1	R
	2748	nov_1_1	F
25	2749	nov_1_1	R
	2750	wzt_1_1	F
	2751	wzt_1_1	R
	2752	wbbl_1_1	F
30	2753	wbbl_1_1	R
	2754	norA23_1_1	F
	2755	norA23_1_1	R
35	2756	mexR_1_1	F
	2757	mexR_1_1	R
	2758	arr2_1_1	F
	2759	arr2_1_1	R
40	2760	mreA_1_1	F
	2761	mreA_1_1	R
	2762	I-cadC_1_1	F
45	2763	I-cadC_1_1	R
	2764	uvrA_1_1	F
	2765	uvrA_1_1	R
	2766	CRD2_1_1	F
50	2767	CRD2_1_1	R
	2768	CDR1_1_1	F
	2769	CDR1_1_1	R
55	2770	CDR1_2_1	F
	2771	CDR1_2_1	R
	2772	MET3_1_1	F

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	2775	FET3_1_1	R
	2776	FTR2_1_1	F
10	2777	FTR2_1_1	R
	2778	MDR1-7_1_1	F
	2779	MDR1-7_1_1	R
15	2780	ERG11_1_1	F
	2781	ERG11_1_1	R
	2782	SEC20_1_1	F
	2783	SEC20_1_1	R
20	2784	rbcL_1_1	F
	2785	rbcL_1_1	R
	2786	LDHA(hu)_1_1	F
25	2787	LDHA(hu)_1_1	R
	2788	GAPD(hu)_1_1	F
	2789	GAPD(hu)_1_1	R
	2790	b-Act(hu)_1_1	F
30	2791	b-Act(hu)_1_1	R
	2792	ARHGDIA(hu)_1_1	F
	2793	ARHGDIA(hu)_1_1	R
35	2794	PGK1(hu)_1_1	F
	2795	PGK1(hu)_1_1	R
	2796	rbcL_1_2	F
	2797	rbcL_1_2	R
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	2799	16SPa_1_1	R
	2800	23SEfaecium_2_1	F
45	2801	23SEfaecium_2_1	R
	2802	16SStrepyog_1_1	F
	2803	16SStrepyog_1_1	R
	2804	16SStrepneu_1_1	F
50	2805	16SStrepneu_1_1	R
	2806	16SStrepagalactiae_1_1	F
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	2809	16SEfaecium_1_1	R
	2810	16SEfaecium_2_1	F

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	2813	16SRNAEf_2_1	R
	2814	16SKpn_1_1	F
10	2815	16SKpn_1_1	R
	2816	16SSa_3_1	F
	2817	16SSa_3_1	R
45	2818	16SRNAEf_1_1	F
15	2819	16SRNAEf_1_1	R
	2820	16SShominis_1_1	F
	2821	16SShominis_1_1	R
20	2822	16SShaemolyt_1_1	F
	2823	16SShaemolyt_1_1	R
	2824	23SEfaecium_1_1	F
25	2825	23SEfaecium_1_1	R
	2826	16SrRNAPrmi_1_1	F
	2827	16SrRNAPrmi_1_1	R
	2828	16SrRNAPrvu1_1_1	F
30	2829	16SrRNAPrvu1_1_1	R
	2830	16SSa_1_1	F
	2831	16SSa_1_1	R
35	2832	16SKlox_1_1	F
	2833	16SKlox_1_1	R
	2834	p53_1_1	F
	2835	p53_1_1	R
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	2837	0135mihck_1_1	R
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#### Claims

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- A DNA microarray for direct identification and characterisation of microorganisms in a sample or clinical specimen, wherein the microarray comprises gene probes being derived from DNA sequences or partial DNA sequences of the microorganisms to be identified or DNA sequences complementary or homologous thereto, and having a length of at least 100 nucletides (nt).
- 2. The DNA microarray of claim 1, wherein
  - (i) the length of the gene probes is from 100 to 1000 nt, preferably from 200 to 800 nt; and/or
  - (ii) the gene probes are specific for a specific microbial species or group of microorganisms to be identified and preferably are DNA sequences selected from the groups consisting of (a) species specific gene probes, (b) virulence gene probes and (c) resistance gene probes; and/or
  - (iii) the microorganisms to be detected are microorganisms which cause bacteremia, fungemia or sepsis and include bacteria and fungi, preferably the microorganisms are selected from the group consisting of *Candida albicans*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneum oniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus lugdunensis*, *Staphylococcus warneri*, *Streptococcus agalactiae*, *Streptococcus bovis*, *Streptococcus dysgalactiae*, *Streptococcus mitis*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, most preferably are *S. aureus*, *E. coli* and/or *P. aeruginosa*; and/or (iv) the sample is selected from whole blood, serum, urine, saliva, liquor, sputum, punktate, stool, pus, wound fluid, positive blood cultures, preferably is positive blood cultures; and/or
  - (v) the array further comprises DNA sequences selected from the group (d) consisting of control gene probes coding for negative controls and positive controls.
- 3. The DNA microarray of claim 2, which is suitable for identification of bacteremia, fungemia or sepsis and wherein the set of gene probes preferably comprises gene probes selected from
- (a) species specific gene probes for
  - (i) Staphylococcus aureus including gene probes derived from cataSaur, clfA, clfB, coa, I-clpC, I-clpP, I-ctaA, I-ctsR, I-dltA, I-dltB, I-dltC, I-dnaK, I-elkT, I-femD, I-glnA, I-glnR, I-grlA, I-grlB, I-groEL, I-groES, I-hemA, I-hemE, I-hemH, I-hemL, I-hemY, I-lepA, I-lrgA, I-lrgB, I-lytM, I-menB, I-menD, I-menE, I-menF, I-mreB, I-mreR, I-mutL, I-mutS, I-NAG, I-pbg, I-pbpF, I-pdhB, I-pdhC, I-rsbU, I-rsbV, I-rsbW, I-sgp, I-sirR, I-sodA, I-sodB, I-sstA, I-sstB, I-sstC, I-sstD, I-trx, I-yhiN, epiP-bsaP, geh, gyrA, gyrB, hemB, hemC, hemD, hemN, hsdS, hsdS, lip, menC, nuc, pdhD, rpoB, SAV0431, SAV0439, SAV0440, SAV0441, sigB, spa, sstC, tag, tyrA, I-aroC, I-aroA, I-cna, I-ebpS, I-eno, I-fbpA, I-fib, I-fnbB, I-srtA, I-stpC, I-fnbA, I-spa, I-aroE, I-aroF, I-aroG, I-asp23, I-atl;
  - (ii) Escherichia coli including gene probes derived from b1169, envZ, fliCb, nfrB, nlpA, pilAe, yacH, yagX, ycdS, yciQ, ymcA;
  - (iii) Staphylococcus epidermidis including gene probes derived from ardeSE0106, ardeSE0107, aroiSE0105, atlE, agrB, agrC, alphSE1368, gad, glucSE1191, hsp10, icaA, icaB, mvaSSepid, nitreSE1972, nitreSE1974, nitreSE1975, oiamtSE1209, ORFISepid, ORF3bSepid, qacR, sin, ureSE1861, ureSE1863, ureSE1864, ureSE1865, ureSE1867;
  - (iv) Staphylococcus haemolyticus including gene probes derived from folQShaemolyt, m vaCShaem olyticus, mvaDShaemolyt, mvaK1Shaemolyticus, m vaSShaem olyticus, RNApolsigm;
  - (v) Staphylococcus lugdunensis including gene probes derived from agrB2Stalugd, agrC2Stalugd, agrC-Stalugd, slam Stalugd;
  - (vi) Staphylococcus warneri including gene probes derived from msrw1Stwar, nukMStwar, proDStwar, proMStwar, sigrpoStwar, tnpStwar;
  - (vii) Candida albicans including gene probes derived from ARG56, ASL43f, BGL2, CACHS3, CCT8, CDC37, CEF3, CHS1, CHS2, CHS4, CHS5, CHT1, CHT2, CHT4, CSA1, 5triphosphatase, AAF1, ADH1, ALS1, ALS7, EDT1, ELF, ESS1, FAL1, GAP1, GNA1, GSC1, GSL1, HIS1, HTS1, HWP1, HYR1, INT1a, KRE15f, KRE6, KRE9, MIG1, MLS1, MP65, NDE1, PFK2, PHR1, PHR2, PHR3, PRA1, PRS1, RBT1, RBT4, RHO1, RNR1, RPB7, RPL13, RVS167, SHA3, SKN1, SRB1, TCA1, TRP1, YAE1, YRB1, YST1exon2:
  - (viii) Enterococcus faecalis including gene probes derived from arcA, arcC, bkdA, cad, camE1, csrA, dacA,

- dfr, dhoD1a, ABC-eltA, agrBfs, agrCfs, dnaE, ebsA, ebsB, eep, efaR, gls24\_glsB, gph, gyrAEf, metEf, mntHCb2, mob2, mvaD, mvaE, parC, pcfG, phoZ, polC, ptb, recS1, rpoN, tms, tyrDC, tyrS;
- (ix) Enterococcus faecium including gene probes derived from bglB, bglR, bglS, efmA, efmB, efmC, mreC, mreD, mvaDEfaecium, mvaEEfaecium, mvaK1Efaecium, m vaK2Efaecium, mvaSEfaecium, orf3\_4Efaeciumb, orf6\_7Efaecium, orf7\_8Efaecium, orf9\_10Efaecium;
- (x) Klebsiella pneumonia including gene probes derived from atsA, atsB, budC, citA, citW, citX, dalD, dalK, dalT, acoA, acoB, acoC, ahlK, fimK, glfKPN2, ltrA, mdcC, mdcF, mdcH, mrkA, mtrK, nifF, nifK, nifN, tyrP, ureA, wbbO, wza, wzb, wzmKPN2, wztKPN2, yojH, liac;
- (xi) Klebsiella oxytoca including gene probes derived from cymA, cymD, cymE, cymH, cymI, cymJ, ddrA, fdt-1, fdt-2, fdt-3, gatY, hydH, masA, nasA, nasE, nasF, pehX, pelX, tagH, tagK, tagT;
- (xii) Pseudomonas aeruginosa including gene probes derived from glpR, lasRb, OrfX, pa0260, pa0572, pa0625, pa0636, pa1046, pa1069, pa1846, pa3866, pa4082, pilAp, PilAp2, pilC, PstP, purK, uvrDII, vsml, vsmR, xcpX;
- (xiii) Streptococcus pneumoniae including gene probes derived from cap1EStrpneu, cap1FStrpneu, cap1GStrpneu, cap3AStrpneu, cap3BStrpneu, celAStrpneu, celBStrpneu, cglAStrpneu, cglBStrpneu, cglCStrpneu, cglDStrpneu, cinA, cps14EStrpneum, cps14FStrpneum, cps14GStrpneum, cps14H-Strpneum, cps19aHStrpneum, cps19alStrpneum, cps19aKStrpneum, cps19f-GStrpneum, cps23fGStrpneum, dexB, dinF, 1760Strpneu, acyPStrpneu, endAStrpneu, exoAStrpneu, exp72, fnlAStrpneu, fnlBStrpneu, fnlCStrpneu, gct18Strpneum, hexB1, hftsHstrpneu, immunofrag1Strpneu, immunofrag-2Strpneu, immunofrag3Strpneu, kdtBStrpneu, lysAStrpneu, pcpBStrpneu, pflCStrpneu, plpA, prtA1Strpneu, pspC1Strpneu, pspC2, purRStrpneu, pyrDAStrpneum, SP0828Strpneu, SP0830Strpneu, SP0833Strpneu, SP0837\_38-Strpneu, SP0839Strpneu, ugdStrpneu, uncC, vicXStrepneu, wchA6bStrpneum, wci4Strpneum, wciK4Strpneum, wciL4Strpneum, wciN6bStrpneum, wciO6b-Strpneum, wciP6bStrpneum, wciY18Strpneum, wzdbStrpneum, wze6b-Strpneum, wzy18Strpneum, wzy4Strpneum, wzy6bStrpneum, xpt;
- (xiv) Streptococcus agalactiae including gene probes derived from cpsA1Strgal, cpsB1Strgal, cpsC1Strgal, cpsD1Strgal, cpsE1Strgal, cpsG1Strgal, cpsIStragal, cpsIStragal, cpsKStragal, cpsMStragal, cpsYStragal, cpsIStragal, cpsIStraga, cylIStraga, cylIStra
- (xv) Streptococcus pyogenes including gene probes derived from cyclStrpyog, fah\_rph\_hlo\_Strpyog, int, int315.5, murEStrpyog, oppA, oppCStrpyog, oppD, SPy0382Strpyog, SPy0390Strpyog, SpyM3\_1351, vicXStrpyog;
- (xvi) Streptococcus viridans including gene probes derived from 573Stprmut, 580SStprmut, 581\_582SStprmut, 584SStprmut, dltAStrmut, dltBStrmut, dltCppx1Strmut, dltDStrmut, lichStrbov, lytRSt-prmut, lytSStprmut, pepQStrrmut, pflCStrmut, recNStprmut, ytqBStrmut;
- (xvii) Proteus mirabilis including gene probes derived from atfA, atfB, atfC, ccmPrmi1, cyaPrmi, aad, flfB, flfD, flfN, flhD, floA, ftsK, gstB, hemCPrmi, hemDPrmi, hev, katA, lpp1, menE, mfd, nrpA, nrpB, nrpG, nrpT, nrpU, pat, pmfA, pmfC, pmfE, ppaA, rsbA, rsbC, speB, stmA, stmB, terA, terD, umoA, umoB, umoC, ureR, xerC, ygbA;
- (xviii) Proteus vulgaris including gene probes derived from envZPrvu, frdC, frdD, infBPrvu, lad, tna2; and/or

#### (b) virulence gene probes for

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- (i) Staphylococcus aureus including gene probes derived from bsaE, bsaG, cap5h, cap5i, cap5j, cap5k, cap8H, cap8I, cap8J, cap8K, I-hId, I-hysA, I-IgGbg, EDIN, eta, etb, hglA, hglB, hglC, hIa, hIb, lukF, lukS, NAG, sak, sea, seb, sec1, seg, seh, sel, set15, set6, set7, set8, sprV8, tst, I-sdrC, I-sdrD, I-sdrE;
- (ii) Escherichia coli including gene probes derived from b1202, eae, eltB, escR, escT, escU, espB, fes, fteA, hlyA, hlyB, iucA, iucB, iucC, papG, rfbE, shuA, SLTII, toxA-LTPA, VT2vaB;
- (iii) Staphylococcus epidermidis including gene probes derived from gcaD, hld\_orf5, icaC, icaD, icaR, psm\_beta1and2, purR, spoVG, yabJ;
- (iv) Staphylococcus haemolyticus including gene probes derived from lipShaemolyt;
- (v) Staphylococcus lugdunensis including gene probes derived from fblStalugd, slushABCStalugd;
- (vi) Staphylococcus warneri including gene probes derived from gehAStwar;
- (vii) Candida albicans including gene probes derived from CCN1, CDC28, CLN2, CPH1, CYB1, EFG1, MNT1, RBF1, RBF1, RIM101, RIM8, SEC14, SEC4, TUP1, YPT1, ZNF1 CZF1;
- (viii) Enterococcus faecalis including gene probes derived from asa1, asp1, cgh, cylA, cylB, cyll, cylL\_cylS, cylM, ace, ef00108, ef00109, ef0011, ef00113, ef0012, ef0022, ef0031, ef0032, ef0040, ef0058,

- enlA, esa, esp, gelE, groEL, groES, rt1, sala, salb, sea1, sep1, vicK, yycH, yycl, yycJ;
- (ix) Enterococcus faecium including gene probes derived from entA\_entI, entD, entR, oep, sagA;
- (x) Klebsiella pneumonia including gene probes derived from cim, aldA, hemly, pSL017, pSL020, rcsA, rmlC, rmlD, waaG, wbbD, wbbM, wbbN, wbdA, wbdC, wztKpn, yibD;
- (xi) P. aeruginosa including gene probes derived from aprA, aprE, ctx, algB, algN, algR, ExoS, fpvA, lasRa, lipA, lipH, Orf159, Orf252, pchG, PhzA, PhzB, PLC, plcN, plcR, pvdD, pvdF, pyocinS1, pyocinS1im, pyocinS2, pys2, rbf303, rhlA, rhlB, rhlR, TnAP41, toxA;
- (xii) Streptococcus pneumoniae including gene probes derived from igaStrpneu, lytA, nanA, nanBStrpneu, pcpCStrpneu, ply, prtAStrpneu, pspA, SP0834Strpneu, sphtraStrpneu, wciJStrpneu, wziyStrpneu, wzx-Strpneu;
- (xiii) Streptococcus agalactiae including gene probes derived from CAMPfactor, 0499Straga, hylStragal, lipStragal;
- (xiv) Streptococcus pyogenes including gene probes derived from DNaselStrpyog, fba2Strpyog, fhuAS-trpyog, fhuB1Strpyog, fhuDStrpyog, fhuGStrpyog, hylA, hylP, hylp2, oppB, ropB, scpAStrpyog, sloStrpyog, smez-Strpyog, sof, speA, speB2Strpyog, speCStrpyog, speJStrpyog, srtBStrpyog, srtCStrpyog, srtEStrpyog, srtFStrpyog, srtGStrpyog, srtKStrpyog, srtRStrpyog, srtTStrpyog, vicKStrpyog;
- (xvi) Streptococcus viridans including gene probes derived from hlyXStrmut, igaStrmitis, igaStrsanguis, perMStrmut;
- (xvii) Proteus mirabilis including gene probes derived from flaA, laD, fliA, hpmA, hpmB, IpsPrmi, mrpA, mrpB, mrpC, mrpD, mrpE, mrpF, mrpG, mrpH, mrpI, mrpJ, patA, putA, uca, ureDPrmi, ureEPrmi, ureFPrmi, zapA, zapB, zapD, zapE; and/or
- (c) resistance gene probes derived from genes coding for

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- (i) beta-lactams resistance including gene probes derived from blaIMP-7, meclSepid, blaOXA-10, blaB, ampC, I-blaR, blaOXA-32, bla-CTX-M-22, pbp2aStrpneu, blaSHV-1, blaOXA-2, blaRShaemolyt, blaIMP-7, I-mecR, blaOXY, dacCStrpyog, femA, mecA, blaIShaemolyt, blavim, pbp2b, pbp2prim eSepid, pbp2x, pbp3Saureuc, pbp4, pbp5Efaecium, pbpC, I-mecI, pbp1a, I-blaI, blaTEM-106, blaOXY-KLOX, ftsWEF, fmhB, cumA, femBShaemolyt, blaPER-1, bla\_FOX-3, blaA, psrb, fmhA, mecR1Sepid, blaZ, blaOXA-1, fox-6, blaPrmi;
- (ii) aminoglycosides resistance including gene probes derived from aacA\_aphDStwar, aacC1, aacC2, strB, aadA, aadB, aadD, aacA4, strA, aph-A3, aacC1, aacA4, aacA-aphD, I-spc, aphA3;
- (iii) macrolides-lincosamines-streptogramins resistance including gene probes derived from ermC, linB, satSA, mdrSA, I-linA, ermB, ermA, satA, msrA, mphBM, mefA, mrx;
- (iv) trimethoprim resistance including gene probes derived from dfrA, dfrStrpneu;
- (v) chloramphenicol resistance including gene probes derived from cat, catEfaecium, cmlA5;
- (vi) tetracyclines resistance including gene probes derived from tetAJ, tetL, tetM
- (vii) glycopeptides resistance including gene probes derived from vanH(tn), vanA, vanHB2, vanR, vanRB2, vanS(tn), vanSB2, vanVllB2, ddl, ble, vanXB2, vanY(tn), vanYB2, vanB, vanZ(tn), vanC-2, vanX(tn);
- (viii) multiple target resistance including gene probes derived from acrB, m exB, I-qacA, sull, sul, cadB-Stalugd, mexA, acrB, emeA, acrA, rtn, abcXStrpmut, qacEdelta1, elkT-abcA, I-cadA, albA, wzm, msrCb, nov, wzt, wbbl, norA23, mexR, arr2, mreA, I-cadC, uvrA;
- (ix) fungicide resistance, especially *C. albicans* fungicide resistance, including gene probes derived from *CRD2*, *CDR1*, *MET3*, *FET3*, *FTR2*, *MDR1-7*, *ERG11*, *SEC20*.
- 4. The DNA microarray of claim 2 or 3, wherein
  - (i) the array comprises the minimal number of species specific gene probes of group (a) which is sufficient for species identification, preferably the array comprises at least 2 different gene probes per target species of group (a); and/or
  - (ii) the array comprises the minimal number of virulence gene probes of group (b) sufficient for virulence determination, preferably at least 1 gene probe, more preferably at least 5 different gene probes per target species of group (b); and/or
  - (iii) the array comprises the minimal number of resistance gene probes of group (c) sufficient for determination of resistance, preferably at least 1 gene probe, more preferably at least 5 different gene probes of group (c); and/or (iv) the DNA sequences are selected from the group consisting of SEQ ID NOs 1-918, complementary sequences thereto, addition mutants, deletion mutants, substitution mutants and homologues thereof.

### 5. The DNA microarray of claim 4, wherein

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- (i) the gene probes of group (a) are selected from SEQ I D NO: 1-99, 142-152, 174-199, 209-214, 216-219, 222-229, 231-291, 308-342, 377-393, 399-431, 449-490, 523-591, 606-639, 645-656, 687-701, 706-749 and 776-781;
- (ii) the gene probes of group (b) are selected from SEQ ID NO: 100-141, 153-173, 200-208, 215, 220-221, 230, 292-307, 343-376, 394-398, 432-448, 491-522, 592-605, 640-644, 657-686, 702-705, 750-775 and 782-784; and/or
- (iii) the gene probes of group (c) are selected from SEQ ID NO:785-918, preferably from SEQ ID NO:785-882.

## 6. The DNA microarray of claim 4 or 5, which

- (I) is suitable for identification of *Staphylococcus aureus* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:1-99, preferably comprises at least the gene probes represented by SEQ ID NO:71 and 68: and/or
- (II) is suitable for identification of *Escherichia coli* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:142-152, preferably at least the gene probes represented by SEQ ID NO:143 and 149; and/or
- (III) is suitable for identification of *Staphylococcus epidermidis* and comprises gene probes of group (a) selected from SEQ ID NO:174-199, preferably at least the gene probes represented by SEQ ID NO:177 and 184; and/or (IV) is suitable for identification of *Staphylococcus haemolyticus* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:209-214, preferably at least the gene probes represented by SEQ ID NO:209 and 210; and/or
- (V) is suitable for identification of *Staphylococcus lugdunensis* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:216-219, preferably at least the gene probes represented by SEQ ID NO:216 and 219; and/or
- (VI) is suitable for identification of *Staphylococcus warneri* and comprises one or more or all of the gene probes of group (a) selected from SEQ I D NO: 224-229, preferably at least the gene probes represented by SEQ ID NO: 224 and 225; and/or
- (VII) is suitable for identification of *Candida albicans* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:231-291, preferably at least the gene probes represented by SEQ ID NO: 231 and 232; and/or
- (VIII) is suitable for identification of *Enterococcus faecalis* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:308-342, preferably at least the gene probes represented by SEQ ID NO:308 and 310; and/or
- (IX) is suitable for identification of *Enterococcus faecium* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:377-393, preferably at least the gene probes represented by SEQ ID NO:377 and 380; and/or
- (X) is suitable for identification of *Klebsiella pneumonia* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:399-431, preferably at least the gene probes represented by SEQ ID NO:399 and 402; and/or
- (XI) is suitable for identification of *Klebsiella oxytoca* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:449-469, preferably at least the gene probes represented by SEQ ID NO: 449 and 455; and/or
- (XII) is suitable for identification of *Pseudomonas aeruginosa* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:470-490, preferably at least the gene probes represented by SEQ ID NO:470 and 471; and/or
- (XIII) is suitable for identification of *Streptococcus pneumoniae* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:523-591, preferably at least the gene probes represented by SEQ ID NO:523 and 524; and/or
- (XIV) is suitable for identification of *Streptococcus agalactiae* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:606-639, preferably at least the gene probes represented by SEQ ID NO:606 and 619; and/or
- (XV) is suitable for identification of *Streptococcus pyogenes* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:645-656, preferably at least the gene probes represented by SEQ ID NO:645 and 646; and/or
- (XVI) is suitable for identification of *Streptococcus viridans* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:687-701, preferably at least the gene probes represented by SEQ ID

NO:687 and 691; and/or

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(XVII) is suitable for identification of *Proteus mirabilis* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:706-749, preferably at least the gene probes represented by SEQ ID NO: 706 and 710; and/or

(XVIII) is suitable for identification of *Proteus vulgaris* and comprises one or more or all of the gene probes of group (a) selected from SEQ ID NO:776-781, preferably at least the gene probes represented by SEQ ID NO:776 and 777.

- 7. The DNA microarray of claim 6, which further comprises
  - (I) for the characterisation of *Staphylococcus aureus*: one or more or all of the gene probes of group (b) selected from SEQ ID NO:100-141, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or (II) for the characterisation of *Escherichia coli*: one or m ore or all of the gene probes of group (b) selected from SEQ ID NO:153-173, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or
  - (III) for the characterisation of *Staphylococcus epidermidis:* one or more or all of the gene probes of group (b) selected from SEQ I D NO:200-208, and/or of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or
  - (IV) for the characterisation of *Staphylococcus haemolyticus*: one or more or all of the gene probe of group (b) represented by SEQ I D NO:215, and/or of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or
  - (V) for the characterisation of *Staphylococcus lugdunensis:* one or more or all of the gene probes of group (b) selected from SEQ ID NO:220-221, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or
  - (VI) for the characterisation of *Staphylococcus warneri:* one or more or all of the gene probe of group (b) represented by SEQ I D NO:230, and/or of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or
  - (VII) for the characterisation of *Candida albicans*: one or more or all of the gene probes of group (b) selected from SEQ I D NO:292-307, and/or of the gene probes of group (c) selected from SEQ ID NO:910-918; and/or (VIII) for the characterisation of *Enterococcus faecalis*: one or more or all of the gene probes of group (b) selected from SEQ I D NO:343-376, and/or of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or
  - (IX) for the characterisation of *Enterococcus faecium*: one or more or all of the gene probes of group (b) selected from SEQ I D NO:394-398, and/or of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or (X) for the characterisation of *Klebsiella pneumonia*: one or more or all of the gene probes of group (b) selected from SEQ ID NO:432-448, and/or of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or (XI) for the characterisation of *Klebsiella oxytoca*: one or more or all of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or
  - (XII) for the characterisation of *Pseudomonas aeruginosa:* one or more or all of the gene probes of group (b) selected from SEQ ID NO:491-522, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or
  - (XIII) for the characterisation of *Streptococcus pneumoniae:* one or more or all of the gene probes of group (b) selected from SEQ I D NO:592-605, and/or of the gene probes of group (c) selected from SEQ I D NO:785-909; and/or
  - (XIV) for the characterisation of *Streptococcus agalactiae:* one or more or all of the gene probes of group (b) selected from SEQ ID NO:640-644, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or
  - (XV) for the characterisation of *Streptococcus pyogenes*: one or more or all of the gene probes of group (b) selected from SEQ ID NO:657-686, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or
  - (XVI) for the characterisation of *Streptococcus viridans:* one or more or all of the gene probes of group (b) selected from SEQ ID NO:702-705, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or
  - (XVII) for the characterisation of *Proteus mirabilis:* one or more or all of the gene probes of group (b) selected from SEQ ID NO:750-775, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909; and/or (XVIII) for the characterisation of *Proteus vulgaris:* one or more or all of the gene probes of group (b) selected from SEQ ID NO:782-784, and/or of the gene probes of group (c) selected from SEQ ID NO:785-909.
- 8. Use of the DNA microarray of any of claims 1 7 for in vitro identification and characterisation of microorganisms

in a sample or in a clinical specimen, preferably for the diagnosis of bacteremia or sepsis.

- An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen comprising
  - (a) isolating the total DNA from the sample or clinical specimen and labelling the DNA with a reporter molecule;
  - (b) applying the DNA thus obtained to the DNA microarray of anyone of claims 1-7 and hybridising the DNA with the gene probes of the DNA m icroarray; and
  - (c) detecting DNA bound to the DNA microrarray by determination of the amount of the reporter molecules bound to the array.
- 10. The method of claim 9,
  - (i) which is a method for diagnosis of bacteremia, fungemia or sepsis; and/or
  - (ii) wherein the clinical specimen is a positive blood culture; and/or
  - (iii) wherein the ratio of microbial DNA to total DNA isolated from said sample or clinical specim en is less than 100 %, preferably from 1% to 99%; and/or
  - (iv) wherein the reporter molecule is a fluorochrome; and/or
  - (v) wherein the determination of the amount of reporter molecules bound to the array is achieved by visualization of the reporter molecule; and/or
  - (vi) wherein the DNA isolated in step (a) is labelled and applied to the DNA microarray without prior amplification.
- 11. A kit for detection of microorgamisms in a sample or clinical specimen comprising the microarray of anyone of claims 1 to 7.

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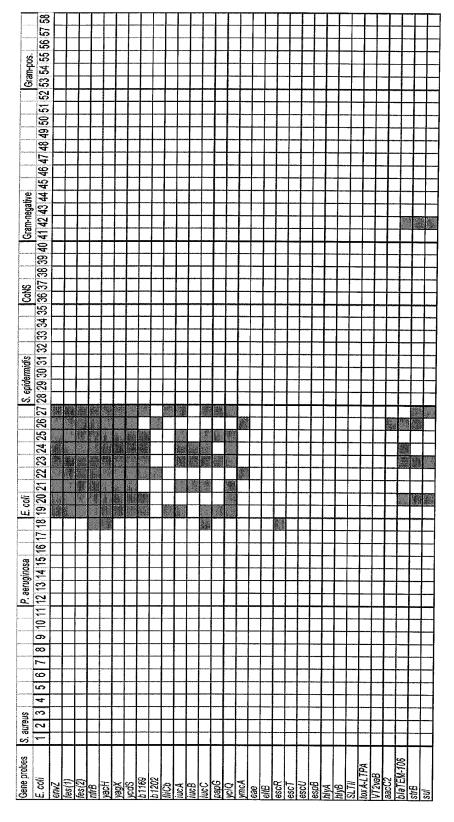
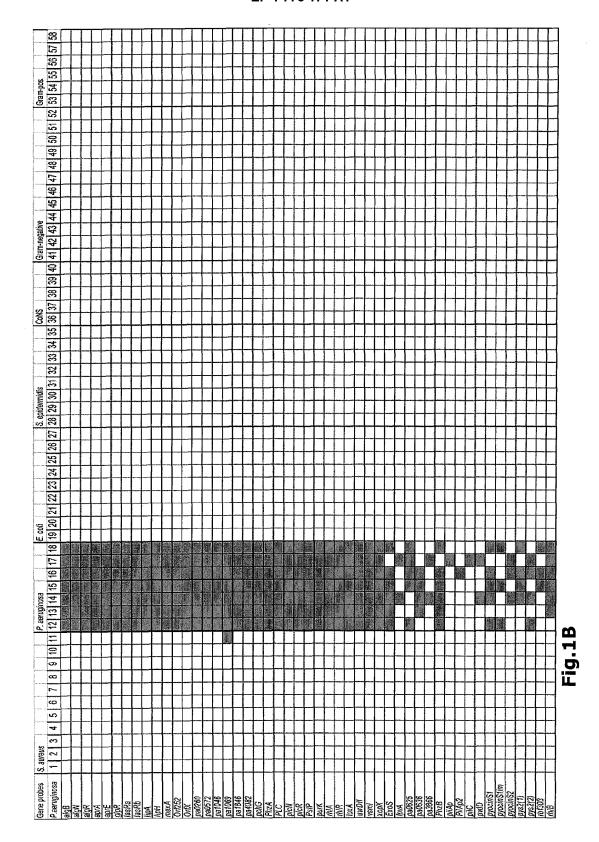


Fig. 1A



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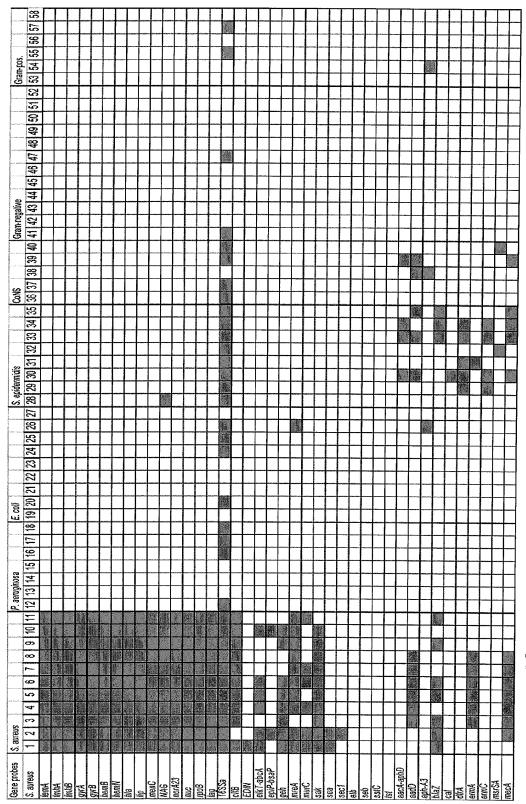


Fig. 10

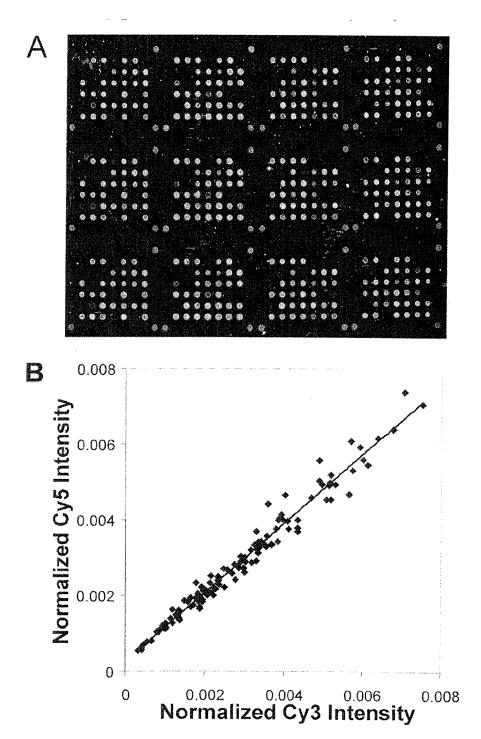


Fig.2

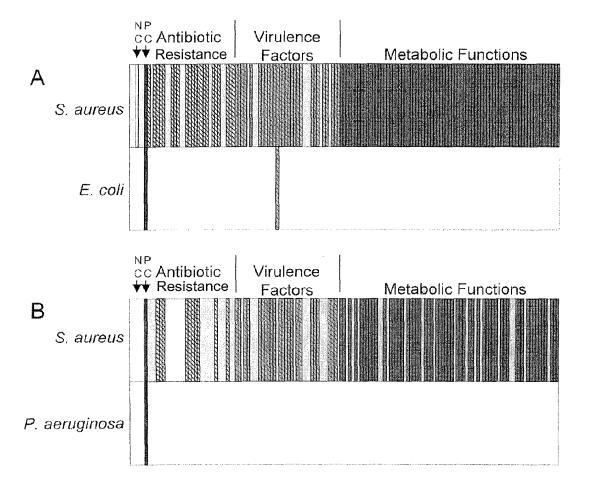


Fig.3

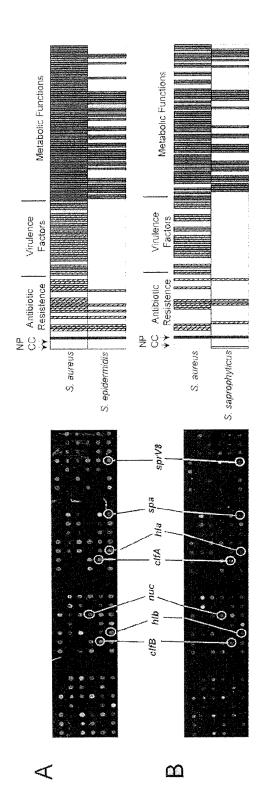
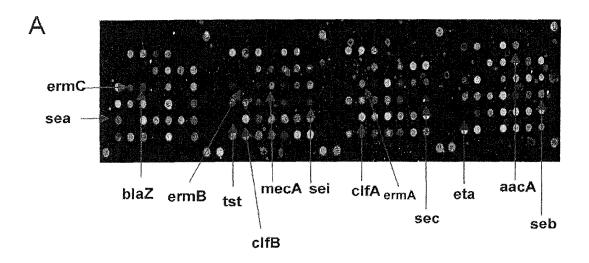


Fig.4



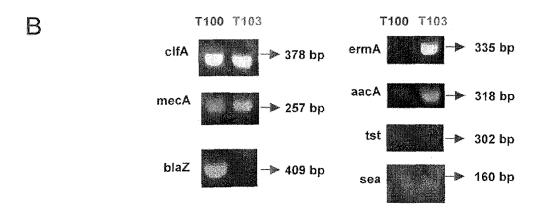
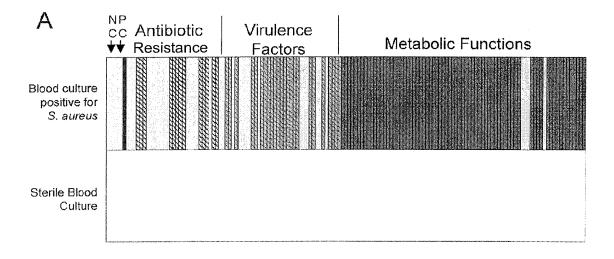


Fig.5



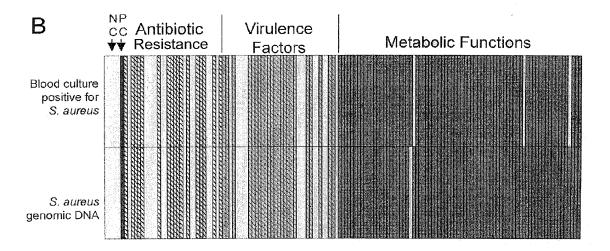


Fig.6



# PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention EP  $\,05\,$  10  $\,9025\,$  shall be considered, for the purposes of subsequent proceedings, as the European search report

	DOCUMENTO CONOCE	EDED TO DE SEI EMANT		]
		ERED TO BE RELEVANT	D-I	OL ACCIFICATION OF THE
Category	Citation of document with ir of relevant passa	ndication, where appropriate, ges	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	US 6 747 137 B1 (WE 8 June 2004 (2004-6 * paragraph [0244] * paragraphs [0132] * paragraph [0012] * sequence 3589 *	* , [0133] *	1-11	INV. C12Q1/68
Α	MICRO ARRAY FOR IDE INFECTIOUS DISEASE HUMAN" 18 May 2003 (2003-0 THE GENERAL MEETING SOCIETY FOR MICROBI	CAUSACTIVE BACTERIA IN 05-18), ABSTRACTS OF	1-11	
А	EP 1 310 569 A (PRE UNIVERSITY) 14 May * claim 14 *	SIDENT OF GIFU 2003 (2003-05-14) 	1-11	TECHNICAL FIELDS SEARCHED (IPC)
INCO	MPLETE SEARCH			
not compl be carried		application, or one or more of its claims, does/ a meaningful search into the state of the art ca ly, for these claims.		
Claims se	arched incompletely :			
Claims no	t searched :			
Reason fo	or the limitation of the search:			
see	sheet C			
	Place of search	Date of completion of the search		Examiner
	Munich	19 December 2005	Hel	liot, B
X : parti Y : parti docu A : teoh O : non-	NTEGORY OF CITED DOCUMENTS oularly relevant if taken alone oularly relevant if combined with anoth ment of the same category nological background written disclosure mediate document	L : document cited fo	oument, but publice en the application or other reasons	shed on, or



# PARTIAL EUROPEAN SEARCH REPORT

Application Number

EP 05 10 9025

	DOCUMENTS CONSIDERED TO BE RELEVANT	_	CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	WO 92/07096 A (MICROPROBE CORPORATION) 30 April 1992 (1992-04-30) * page 12, paragraph 2 * * page 27, paragraph 2 * * example 6 *	1-11	
Α	LEHNER A ET AL: "Oligonucleotide microarray for identification of Enterococcus species" 1 May 2005 (2005-05-01), FEMS MICROBIOLOGY LETTERS, AMSTERDAM, NL, PAGE(S) 133-142, XP004876200 ISSN: 0378-1097 * abstract *	1-11	TECHNICAL FIELDS
A	WANG R-F ET AL: "DNA microarray analysis of predominant human intestinal bacteria in fecal samples" August 2004 (2004-08), MOLECULAR AND CELLULAR PROBES, ACADEMIC PRESS, LONDON, GB, PAGE(S) 223-234, XP004522575 ISSN: 0890-8508 * abstract; tables 1,2 *	1-11	SEARCHED (IPC)



## INCOMPLETE SEARCH SHEET C

Application Number

EP 05 10 9025

Claim(s) searched completely: 1-5,7-21

Claim(s) searched incompletely:

Reason for the limitation of the search:

The present remarks apply to the only searched invention. If further search fees were paid, similar remarks could apply to the further searched inventions, leading to an incomplete search.

The present claim 6 relates to an DNA microarray suitable for the detection of Staphylococcus aureus and/or other microorganisms, among them C. albicans, using one or more or all gene probes listed as SEQ ID  $N^{\circ}$  1-909.

However, in view of the extremely large number of possible probes mentioned in the said claim, the said claim 6 lacks clarity and conciseness in the sense of Article 84 and a meaningful search of the whole claimed subject-matter of the claim could not be carried out (Rule 45 EPC and Guidelines B-VIII, 3).

The search of claim 6 was, thus, limited to the only microarray clearly disclosed in the application and suitable for the identification of C. albicans, namely the microarray comprising either the gene probe listed as SEQ ID N° 231 (irrespective of any other probes) or the whole of the genes listed as SEQ ID N° 1-909, and having a length of at least 100 nucleotides.



**Application Number** 

EP 05 10 9025

CLAIMS INCURRING FEES
The present European patent application comprised at the time of filing more than ten claims.
Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.
LACK OF UNITY OF INVENTION
The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:
see sheet B
All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:  1-11 (all partially)



Application Number

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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Invention 1: 1-11 (all partially)

A DNA microarray for direct identification of Candida albicans in a sample or clinical specimen, wherein the microarray comprises the gene probe listed as SEQ ID N $^{\circ}$  231 or the whole of the genes listed as SEQ ID N $^{\circ}$  1-909, and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Inventions 2-85: claims 1-11 (all partially)

A DNA microarray for direct identification of Candida albicans in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N $^\circ$  n (wherein n is an integer comprised between 232 and 307 and between 910 and 918), and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Inventions 86-278: claims 1-11 (all partially)

A DNA microarray for direct identification of Enterococcus faecalis in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N° n (wherein n is an integer comprised between 308 and 376 and between 785 and 909), and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

micai specimen.

Inventions 279-300: claims 1-11 (all partially)



**Application Number** 

EP 05 10 9025

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

A DNA microarray for direct identification of Enterococcus faecium in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N° n (wherein n is an integer comprised between 377 and 398), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Inventions 301-333: claims 1-11 (all partially)

A DNA microarray for direct identification of Escherichia coli in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N° n (wherein n is an integer comprised between 142 and 173) or gene probes as listed in Tab. 2 of Example 4, and having a length of at least 10 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Invention 334: claims 1-11 (all partially)

A DNA microarray for direct identification of Klebsiella oxytoca in a sample or clinical specimen, wherein the microarray comprises gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 449 and 469), and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Inventions 335-384: claims 1-11 (all partially)



Application Number

EP 05 10 9025

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

A DNA microarray for direct identification of Klebsiella pneumoniae in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 399 and 448), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Invention 385: claims 1-11 (all partially)

A DNA microarray for direct identification of Proteus mirabilis and vulgaris in a sample or clinical specimen, wherein the microarray comprises gene probes listed as SEQ ID N $^\circ$  n (wherein n is an integer comprised between 706 and 775 and between 776 and 784), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Invention 386: claims 1-2, 8-11 (all partially)

A DNA microarray for direct identification of Enterobacter cloacae in a sample or clinical specimen.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Inventions 387-439: claims 1-11 (all partially)



Application Number

EP 05 10 9025

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

> A DNA microarray for direct identification of Pseudomonas aeruginosa in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N° n (wherein n is an integer comprised between 470 and 522), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Invention 440: claims 1-2, 8-11 (all partially)

A DNA microarray for direct identification of Stenotrophomonas maltophilia in a sample or clinical specimen.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Invention 441: claims 1-2, 8-11 (all partially)

A DNA microarray for direct identification of Acinetobacter baumannii in a sample or clinical specimen. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Inventions 442-581: claims 1-11 (all partially)

A DNA microarray for direct identification of Staphylococcus aureus in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N° n (wherein n is an integer comprised between 1 and 141), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.



Application Number

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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Inventions 582-616: claims 1-11 (all partially)

A DNA microarray for direct identification of Staphylococcus epidermidis in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 174 and 208), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Invention 617: claims 1-11 (all partially)

A DNA microarray for direct identification of Staphylococcus haemolyticus in a sample or clinical specimen, wherein the microarray comprises gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 209 and 215), and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Invention 618: claims 1-11 (all partially)

A DNA microarray for direct identification of Staphylococcus lugdunensis in a sample or clinical specimen, wherein the microarray comprises gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 216 and 221), and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Invention 619: claims 1-11 (all partially)



**Application Number** 

EP 05 10 9025

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

A DNA microarray for direct identification of Staphylococcus warneri in a sample or clinical specimen, wherein the microarray comprises gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 224 and 230), and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Invention 620: claims 1-11 (all partially)

A DNA microarray for direct identification of Streptococcus agalactiae in a sample or clinical specimen, wherein the microarray comprises gene probes listed as SEQ ID  $N^{\circ}$  n (wherein n is an integer comprised between 606 and 644), and having a length of at least 100 nucleotides. Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Invention 621: claims 1-2, 8-11 (all partially)

A DNA microarray for direct identification of Streptococcus bovis in a sample or clinical specimen.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Invention 622: claims 1-2, 8-11 (all partially)

A DNA microarray for direct identification of Streptococcus dysgalactiae in a sample or clinical specimen.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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Invention 623: claims 1-2, 8-11 (all partially)



Application Number

EP 05 10 9025

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

A DNA microarray for direct identification of Streptococcus mitis in a sample or clinical specimen.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Invention 624: claims 1-2, 8-11 (all partially)

A DNA microarray for direct identification of Streptococcus mutans in a sample or clinical specimen.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Inventions 625-831: claims 1-11 (all partially)

A DNA microarray for direct identification of Streptococcus pneumoniae in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 399 and 605), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

Inventions 832-873: claims 1-11 (all partially)

A DNA microarray for direct identification of Streptococcus pyogenes in a sample or clinical specimen, wherein the microarray comprises one gene probe selected among the gene probes listed as SEQ ID N $^{\circ}$  n (wherein n is an integer comprised between 645 and 686), and having a length of at least 100 nucleotides.

Use of the DNA microarray.

An in vitro method for identification and characterisation of microorganisms in a sample or in a clinical specimen. A kit for the detection of microorganisms in a sample or clinical specimen.

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## ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO.

EP 05 10 9025

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

19-12-2005

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		Α	14-05-2003				
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#### REFERENCES CITED IN THE DESCRIPTION

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